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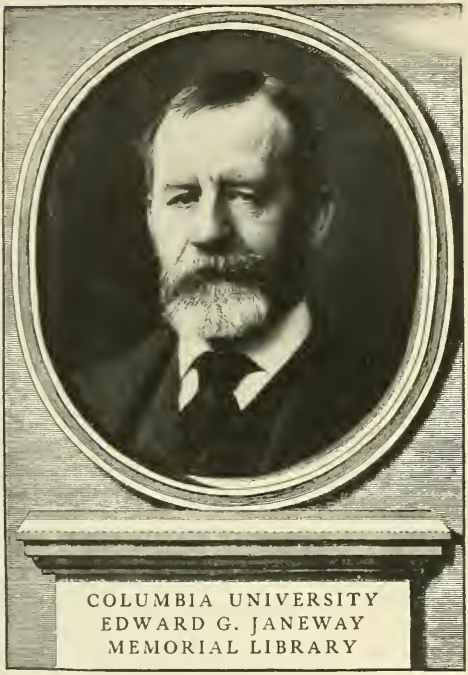

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A MANUAL OF MEDICINE

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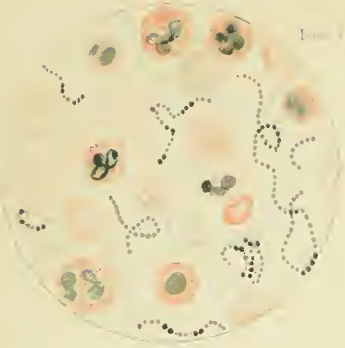

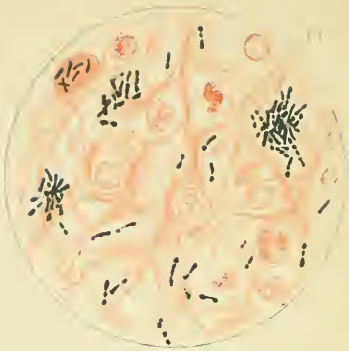

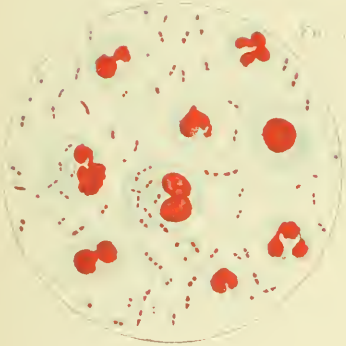

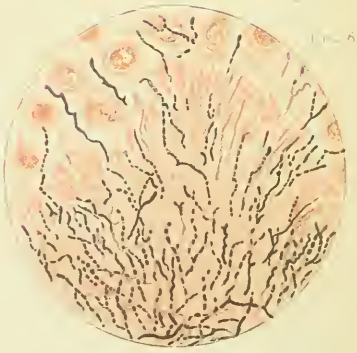

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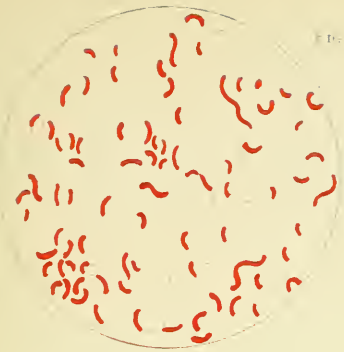

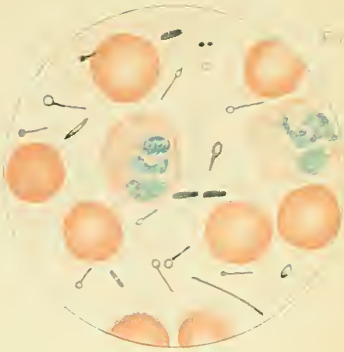

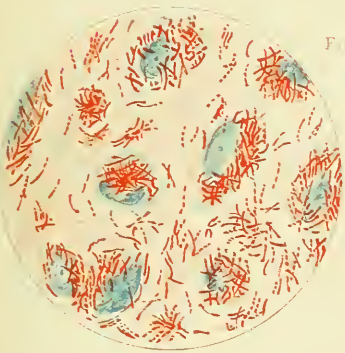

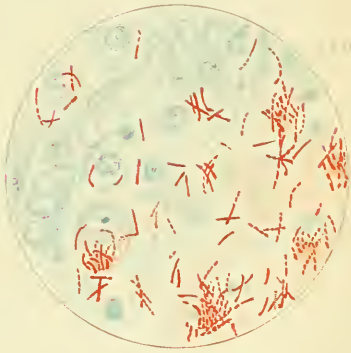

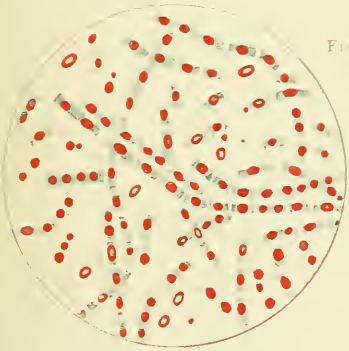

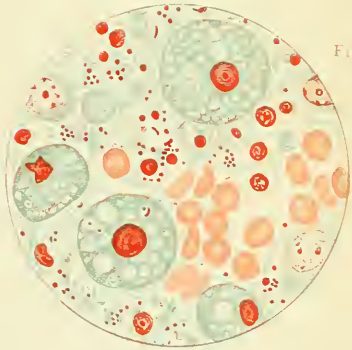

A

MANUAL OF MEDICINE

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VOL. I

GENERAL DISEASES

DISEASES EXCITED BY ATMOSPHERIC INFLUENCES
THE INFECTIONS

New York

THE MACMILLAN COMPANY

LONDON: MACMILLAN & CO., LTD.

1900

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Norwood Press
J. S. Cushing & Co. — Berwick & Smith
Norwood Mass. U.S.A.

TO

THE MEMORY

OF

MY TEACHER

Sir William Jenner, Bart., G.C.B.

M.D., F.R.C.P., F.R.S.

PHYSICIAN IN ORDINARY TO H.M. THE QUEEN, AND

TO H.R.H. THE PRINCE OF WALES

PHYSICIAN TO UNIVERSITY COLLEGE HOSPITAL

W. H. A.

PLATE I.

FIG. 1.

Streptococcus Pyogenes in Pus from case of Empyema. Fixed by Wet Method. Stained with Eosin Alum and Methylene Blue. × 1000 diams.

FIG. 2.

Section of Diphtheria Membrane. Bacillus Diphtheriæ. Stained by Gram's Method and Saffranin. × 1000 diams.

FIG. 3.

Scraping from Septic Pleurisy, showing Fraenkel's Pneumococci with Capsules. Stained by Muir's Method. × 1000 diams.

FIG. 4.

Bacillus of Typhoid Fever showing Flagella. Muir's Stain for Flagella. × 1000 diams.

FIG. 5.

Bacillus of Bubonic Plague. 48 hours' Agar Culture; Flagella seen. Stained by Muir's Method. × 1000 diams.

FIG. 6.

Actinomyces in Liver Abscess, showing Filaments and Clubs. Stained by Gram's Method, Saffranin and Eosin. × 1000 diams.

PLATE II.

FIG. 7.

Koch's Spirillum of Cholera. 12 hours' Agar Culture ; Flagella. Muir's stain for Flagella. × 1000 diams.

FIG. 8.

Bacillus Tetani in scraping from wound (Hand) from case of Tetanus. Fixed by Muir's Method. Stained with Eosin and Methylene Blue.

FIG. 9.

Skin from case of Leprosy. Bacilli stained by Ziehl Neelsen Method, with Methylene Blue for contrast stain. × 1000 diams.

FIG. 10.

Bacillus Tuberculosis in Lung in Acute Tubercular Broncho-pneumonia. Stained by Ziehl Neelsen Method. × 1000 diams.

FIG. 11.

Bacillus Anthracis (Spores). 3 days' Agar Culture. Stained by Ziehl Neelsen Method—Fuchsine and Methylene Blue Method. × 1000 diams.

FIG. 12.

Amœbic Dysentery. Amœbæ in wall of Abscess of Liver. From Specimen kindly supplied by Prof. Greenfield. Fixed by Corrosive Sublimate Method. Stained by Benda Method. × 1000 diams.

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and

The Editor.

(*Diseases due to Atmospheric Influences.*)

A MANUAL OF MEDICINE

INTRODUCTION

The term "Medicine" is generally understood to denote the study of disease in the various directions which engage the attention of the scientific investigator and the practical physician. Therein is included the inquiry into those precedent conditions commonly known as the causes which determine departures from health — the subject of *etiology;* the perversions of structure, macroscopic and microscopic, which the tissues and organs exhibit as the result of these recognised or assumed causes — the department of *morbid anatomy;* the mode of action of disease processes and their effects on the various organs and functions of the body, the forms of malnutrition, general and local — the subject matter of *pathology* in its restricted sense;[1] the signs and symptoms of structural and functional defects; the manifestations of disease as appearing in the living, — the so-called *semeiology* or more commonly *clinical medicine*, in which also is comprised the modes of examination of the patient, the detection of the symptoms, and the drawing of inferences from the evidence so obtained, in short the formation of a *diagnosis* and naming the disease, as well as the expression of a forecast or anticipation of the probable course and ending of the special malady under consideration — the *prognosis;* and finally there is that branch of the subject denominated therapeutics which deals with the *treatment* of disease, by diet, by general hygiene, and by drugs, with the art of its application; to which also may be added the *prevention of disease* and the care of the public health. Extensive as this range of subject matter is, it is far from all that is really involved. The study of disease presupposes a knowledge of the normal, which is

[1] Pathology in its literal significance denotes the study of disease in all its aspects.

a necessary preliminary to the recognition of variations from the standard of health, and for the full pursuit of this wide scope of investigation there is scarcely any department of natural science, from geology and meteorology to botany and zoology, physics and chemistry, which is not in some degree drawn upon to contribute to the elucidation of the complex problems concerned.

It might naturally be supposed that in a work professing to deal with the natural history of disease in its various aspects and many forms, that some explanation of what is meant by "disease" would be attempted, and for the purpose of giving some coherence to the descriptions which are to follow, it is desirable that the attempt should be made, premising that any definition is but provisional and subject to correction as greater precision of knowledge is attained, and is only a working hypothesis for the time being.

Health and *disease* are correlative terms expressive of certain structural and functional states of the body and its workings, distinguished the one from the other by no clearly recognisable line of separation, and neither of them conforming to one fixed and definite type. The standard of bodily health is at present incapable of accurate definition; its borderland, where it merges into disease, cannot be mapped out, whether it be in the direction of structural changes or of functional manifestations, but it is certain that the limits of this standard are wide, and that there are many ways of being well, many types of health. Marked variations from this ill-defined condition constitute disease, the commencements and slighter forms of which can seldom be formulated. In these modes of living three factors are assumed: the bodily structure, its functional activities, and the environment; life, whether normal or morbid, is the resultant of their interaction. By observation or by experience there is recognised a certain range of structure, of function, and of environment, as associated with what it is agreed to regard as healthy life, characterised for the most part by a freedom from pain or discomfort, departures from which are considered as disease. The notion of disease implies no new element, but simply some perversion of the factors that together make up health.

The fundamental conceptions of *structure* and *function* — what the body *is* and what it *does* — are inseparable. We only know the one through the other; we only recognise the material or structure by the properties which it manifests, and conversely the properties are inconceivable apart from the material through which they are rendered sensible.

The connotation of "structure" is not to be restricted to the

results of anatomical investigation, whether gross or minute, whether of the fully-formed organ and tissues or of these in the course of their development and differentiation. The actual disposition and arrangement of the component materials of the body is not bounded by what the microscope discloses. There is a further stage in the inquiry into what a living (as also a non-living) body or any part of such body really is, known as its chemical composition and molecular constitution, and when that is reached the structure of an object in its fullest sense may be regarded as known. "Chemical structure," which implies not only the chemical elements and proportions thereof of which a substance is composed, but also the arrangement of the atoms of these elements in the molecules, and the relations they bear to one another, is the third and final stage of structure, the first and second being gross and minute anatomy respectively. This last stage is still within the realm of theory, but the hypotheses which are current are among the fundamental conceptions upon which all our knowledge of the material world is built.

Inseparable from the idea of structure are the properties by which it is recognised. Such are weight, hardness or softness, flexibility or rigidity, elasticity, permeability and the like, all dependent on the character of the relationships existing between the ultimate constituent molecules of the material. These and others are denominated *physical properties*, and are possessed by all matter, whether living or not. Certain substances, however, over and above these qualities, manifest certain specific properties, in virtue of which they are called *living*, and similarly it is generally assumed that these properties are the outcome of some special molecular structure. These peculiarly vital characteristics may be grouped thus: (1) Those which may be collectively termed "irritability," that is the various forms of response to the application of stimuli (often of external origin) which we recognise as muscular contraction, nervous energy, glandular secretion, together with the power of multiplication and perpetuation of the race by fission, gemmation, etc. (2) Those comprehended in the processes — other than purely chemical — by which the living material increases in bulk and maintains its structural and functional integrity by the conversion of food into its own substance — the nutritive or metabolic processes. (3) Within a variable range, living matter has, as one of its most significant peculiarities, the power of adapting itself to variations of the external conditions subject to which it exists. Within certain limits of temperature, barometric pressure, quality of

food, etc., living things may adjust themselves, beyond which, however, they succumb. A highly specialised phase of this resisting power of the living tissues is known as *immunity*. (4) Lastly, all living things, sooner or later, cease to display these vital characteristics and die.

Much difference of opinion has prevailed as to the nature of these "vital" phenomena. Formerly it was held that life and the manifestations of organism generally were due to a special "vital force" or "principle," fundamentally different from physico-chemical forces, and were not to be investigated by physico-chemical methods. During the last fifty years, however, this vitalistic theory has gradually been displaced by a reference of the manifestations of life to physico-chemical standards, with the important result that very many of the phenomena of the living organism are understood and explained "by comparison with their physical counterparts" (Burdon Sanderson). Extensive and fruitful as the consequences of this procedure have been, there still remain certain living manifestations which are not considered as being capable of either investigation or explanation by these means, which it is further alleged are quite inapplicable. A new vitalism has been recently promulgated, which, accepting to the full all that physico-chemical methods have done in explaining many of the living activities, aims at investigating those which the physico-chemical physiologist tends to regard as unknowable, by the extension to the study of living things of the principle which, in the hands of the morphologists, has elucidated so many problems of structure, viz. "that each part of an organism is determined as regards its mode of existence by its relation to other parts," which is "just as much a physiological as an anatomical conception" (J. Haldane).

Consistent with this view a much wider and indeed truer range of meaning must be attached to the notion of environment than that which restricts it to the mere influence of conditions outside the body, climatic, telluric, dietetic, occupational, etc., important and subtle as these may be. The functional activity of each organ, of each tissue, and of each cell reacts upon these external influences, the effect of which is conditioned by the state of the organism itself. Moreover, the vitality of each structural element is not to be regarded in its origin or its manifestation as independent of the vitality of other constituents of the body, but rather that there should be included in the idea of interaction of organism and environment, the mutual effect of living cells and tissues upon each other.

The notion of disease embodied in the foregoing remarks will show that it involves equally a structural and a functional side. Both aspects are included in the expression. There can be no structural abnormality, however minute, without some functional perversion; and conversely a functional imperfection necessarily implies a structural defect. But just as there are many functional manifestations, both of health and disease, which are not accompanied by any structural change recognisable by the means at present at our command, so many structural abnormalities may be found post-mortem without any functional defect obviously connected therewith.

The conception of life, whether healthy or diseased, as the result of interaction between the organism and its environment, facilitates the comprehension of the direction in which the so-called causes of disease produce their effects. On the one hand, the disturbance of function may be clearly due to faults in the surrounding conditions — food, temperature, occupation, etc. — constituting the *acquired diseases*. On the other, the causation of the morbid states is some inherent defect due to imperfection of the organism as derived from the parents — *hereditary diseases*. It may be that these intrinsic or extrinsic defects are so strong as inevitably to assert themselves and produce disease, or it may be that neither cause may be sufficiently potent to lead to disease of itself, requiring for its efficient action some defect in both. Thus the transmitted liability or tendency to disease may not assert itself until the external conditions have transgressed the limits ordinarily recognised as normal, or that the latter may be inoperative until the resisting powers of the organism have deteriorated. It is a combination of both kinds of faults that is probably responsible for most cases of disease.

So far the general nature of disease; but the perversions of structure and function known as the signs and symptoms of disease are found to occur in groups with more or less constancy and uniformity, constituting the various diseases to which special names are attached, such as epilepsy, typhoid fever, pneumonia. Occasionally, however, obscure cases are met with which do not conform to any of the recognised special diseases, and cannot be named. When the evidences of disease are primarily or mainly confined to one organ or region, the malady is termed *local*, but seldom or never is the disease absolutely so restricted; the rest of the body participates much or little in the abnormal state. If, however, the signs and symptoms are more generally distributed and no organ appears to be predominantly involved, a *general disease* is said to exist. Such a

distinction, however, is in great measure artificial, and, like the notion of separate diseases, is apt to be pushed too far and lead the beginner to expect a definiteness in the several maladies which does not and cannot exist. The descriptions of disease in text-books on medicine unavoidably tend to favour this mistake, which bedside work alone can avert.

The investigation of these various diseases in the living is capable of consideration from two points of view. On the one hand may be taken the description of an individual case, the history of the patient as regards his family, his age, occupation, mode of life, and previous illnesses, whereby an estimate may be formed of his personal health-value in its relation to the special ailment from which he is suffering; the condition of the patient might be set forth, and the progress of the disease to its termination, together with such treatment as may have been followed, and the effect thereof. Such a description would be one of the disease as manifested by that one individual. But it will be readily understood that the disease would exhibit differences in its symptoms and course, and that in no two persons would it be exactly alike, any more than the normal life of the two would be identical. From the consideration of a large number of individual cases, what might be termed a typical or standard or mean account of the malady might be prepared, to which all cases of the same would correspond in the main, differing in detail as the individuals themselves and their conditions of life, constitution, age, and sex would differ. There is, then, besides the *clinical description applicable to each separate case*, a general or *systematic account of each separate malady* collated from a study of many cases. Such an account must necessarily, as knowledge advances and precision of observation extends, be modified from time to time, as the successive editions of current text-books testify. It is well for the student to remember that the description of each disease, as given in systematic treatises, rarely corresponds to any one case, though most cases may be comprehended within it; and since in the time at his disposal it is impossible for him to form for himself anything like a complete account of the various forms of disease from the observation of individual cases, he must depend on the labours of others. It is as supplementary to his clinical work that text-books and systematic lectures have their use.

A systematic account of the principles and practice of medicine necessitates a *classification* of the various morbid states which we are in the habit of regarding as separate diseases. And with classification — nosology — there at once enters into the question an

artificial disposition of the various phenomena, which is constantly undergoing revision, and at the best must be unsatisfactory, since the material to be classified is so many sided and so complex that no plan, within our present knowledge, can effectively arrange the multitudinous varieties of disease without the occasional violation of any principle of grouping, whatever it be, or the rupture of what are apparently the natural affinities between the various maladies. Doubtless the most satisfactory and most scientific arrangement of the groups of phenomena which constitute the various diseases we are familiar with would be based upon their causation, the circumstances and conditions that preceded, and, as we say, determined, the departure from the normal standard of health. But our knowledge of this standard, and still more of the intimate nature and mode of working of the causes, is most imperfect, and at present quite unfit to be made the sole ground of classification, the object of which after all is for convenience of record and study, and at the best most imperfectly represents the natural conditions. Or, consistently with the preceding conception of disease, its varieties might be primarily grouped according to imperfections of the fundamental properties, physico-chemical and vital, which the tissues possess. Thus one group of morbid processes might be due to impaired elasticity, flexibility, permeability, or other such qualities; another to defects in muscular, nervous, or glandular irritability, whether in the direction of excess, of deficiency, or of perversion; a third class of maladies are fundamentally imperfections of the metabolic processes constituting tissue nutrition, whether on the constructive side, that is connected with the due elaboration of the ingesta, or in respect to the subsequent tissue destruction and consequent waste formation and elimination. An altered resisting or adaptive power on the part of one tissue or organ, or of the entire body, characterises a fourth group of infirmities, which would comprise those tissue changes, expressive of a response to an irritant, included within the term "inflammation." And a proneness to degeneration and premature senility or death is the leading feature at the root of others. At present, however, any such scheme is inapplicable; our knowledge would not enable an even approximately complete classification to be made, and for purposes of convenience it would be futile. It is, nevertheless, occasionally advantageous to contemplate the general field of disease, or even of individual cases, from some such standpoint, imperfect though it be.

No scientific principle therefore is to be looked for in the plan here followed. The old-fashioned separation into "general" and

"local" diseases has taken too firm a hold to be lightly discarded in a student's manual, and opinion is not yet prepared for a plan of dealing with the subject which would abolish the time-honoured category of diseases of the various systems of organs, and substituting a grouping under their causal conditions, or as manifestations of general pathological states, rather than under the organs which in many cases, but not always, are mainly or primarily affected. But it may be anticipated that some such arrangement will have to be followed in the future.

It is obviously impossible within the limits of a single work to treat of all of the many sides of this comprehensive subject, and at once some limitation has to be imposed. In the following pages will be found an account of the various forms of disease, more especially from the point of view of their clinical manifestations and treatment. The subjects of etiology and morbid anatomy are briefly summarised, and for further knowledge of these aspects of disease reference must be made elsewhere. The aim has been to present such a picture of the several maladies as will conform to the appearances detected at the bedside, and enable the observer rationally to administer such treatment as our art affords.

THE EDITOR.

GENERAL DISEASES

By general diseases — a phrase of no very precise definition — is meant those maladies in which the entire body is more or less concerned, with no preponderance of symptoms in one region, or where any local manifestations are quite disproportionate or secondary to the widespread disturbance of function. They are either, for the most part, associated with fever and acute in character, or are profound affections of the general nutrition tending to a chronic course and a fatal termination.

A grouping of the diseases comprehended within this category is mainly based on grounds of convenience and on no definite scientific principle. As a provisional arrangement the following plan is adopted: —

I. OF EXTRINSIC CAUSATION.

1. *DISEASES EXCITED BY ATMOSPHERIC INFLUENCES.*
2. *DISEASES CAUSED BY THE INVASION OF LIVING ORGANISMS.*

Vegetable
- *Ectophyta
  e.g. Tinea
- Entophyta
  e.g. Bacilli. Actinomycosis

Animal
- Entozoa
  e.g. Plasmodium Malariæ
  Intestinal and other worms
- *Ectozoa
  e.g. Pediculi

} Infective diseases.

3. *DISEASES DETERMINED BY POISONS INTRODUCED INTO THE BODY AS SUCH.*

e.g. mineral and food poisons, serpent venom. (intoxications.)

II. OF INTRINSIC ORIGIN.

1. *PRIMARY PERVERSIONS OF GENERAL NUTRITION.*
2. *DISEASES OF THE BLOOD.*

* Will be treated of under Diseases of the Skin.

DISEASES EXCITED BY ATMOSPHERIC INFLUENCES

The influence of the various factors of the environment, such as temperature, light, moisture, barometric pressure, electrical states, etc., collectively denominated atmosphere, in the production of disease, is undoubted. Oftenest, perhaps, they act by so impairing the resisting power of the organism as to permit other morbific agents producing their effect; sometimes, however, they appear to be mainly, if not entirely, the excitant of definite morbid states or even of death. Co-existing as they do, it is difficult to appreciate the individual share each may take in the causation of disease, their effect in this direction being more probably a combined one.

1. Temperature

(*a*) Heat. — To excessive heat, whether of the sun directly or in the shade, or artificially produced, are attributed very various conditions, to which the terms "heat-stroke," "sun-stroke" (insolation), or "heat-apoplexy" are indifferently applied. Considerable difference exists in the resisting power of individuals and of races, and habitual exposure usually confers increased tolerance. The ill effects of heat are much intensified by atmospheric moisture — such as occurs in the stoke-holes of steamships — whereby the loss of heat from the skin is much diminished and the regulation of the body temperature consequently interfered with. Other favouring conditions are unsuitable clothing, great physical exertion, alcoholism, heart disease, or other enfeebled states of health. When the exposure takes place in a confined space or crowded room, the vitiated air doubtless contributes to the result.

Symptoms. — The chief clinical distinction among cases of heat-stroke depends upon whether the body temperature of the patient is or is not elevated. Sometimes, however, in the milder non-febrile forms pyrexia may develop.

The leading features of the apyretic cases are extreme exhaustion and tendency to syncope, a subnormal temperature and partial collapse, with vomiting, dilated pupils, and small, quick pulse. Milder degrees of these conditions are familiar to all, from the pleasurable sense of lassitude to the more severe states. In some there are superadded dyspnœa and failing respiration; such cases, being usually more sudden in onset and more fatal, are among those frequently termed "heat apoplexy."

To those cases of heat- or sun-stroke which are marked by hyperpyrexia the names "thermic fever" or "siriasis" are specially applied. All degrees of suddenness of attack are met with, from those who are struck down and die within a few minutes or hours to those in whom for several days before the dangerous symptoms appear there is general weakness, headache, nausea, drowsiness, and frequent and copious micturition.

"Generally," says Dr. Sambon, whose admirably graphic description I quote almost *verbatim* (*Brit. Med. Journ.* 1898, i. p. 744), "patients are seized with severe headache, an alarming sense of general oppression or exhaustion, or difficulty in breathing, and a distressing burning in the eyes, associated with vertigo and chromatopsia (surrounding objects appearing of uniform colour, usually red, blue, or purple). The skin is dry and intensely hot; the patient is pale and excessively thirsty. The pulse is full, rapid, and bounding; respiration is hurried and oppressed. The temperature rises suddenly to 107° or 108°, or even to 112° or higher. Vomiting is very common, and may be a special feature at the outset; purging is, in severe cases, almost always present, the motions being watery and colourless. The skin and breath have a peculiar mousy odour. Cramps in the calves of the legs or in the muscles of the back, sometimes amounting, it is said, to opisthotonos. A maculo-papular eruption has been described as of occasional occurrence, but it is not characteristic. Insensibility soon sets in, from which at first the patient may be roused, but which soon deepens into profound coma. Convulsive twitchings of the facial muscles, or arms, or even general convulsions may be present; but frequently the patient lies motionless from the commencement to the termination of the attack. The reflexes are diminished or abolished. The urine is scanty and often suppressed; it usually contains traces of albumen, a few hyaline or granular casts and blood corpuscles. The breathing becomes almost entirely diaphragmatic; the patient grinds his teeth and moans loudly at each expiration, loud râles and rhonchi being audible over the chest, with cyanosis of the face. The eyes are fixed and turned slightly

upwards; the conjunctivæ are excessively congested, and the pupils are contracted to mere pin points and do not react to light. After a time convulsions and vomiting cease and the patient passes into a state of low muttering delirium; the skin, still hot, becomes clammy; the heart's action becomes more rapid, weaker, and irregular, and the respiration slower and stertorous, or of the Cheyne-Stokes' type, with loud, mucous, tracheal rattling. Frothy mucus, often blood-stained, is ejected by mouth and nostrils, and the patient dies from asphyxia. In favourable cases the temperature falls, the pupils relax, and the patient regains consciousness; the respiration improves and the pulse-rate declines; not uncommonly there is a discharge of urine, after which sleep follows. Termination is usually by crisis, and although the prostration is extreme, convalescence is rapid." The duration of the symptoms varies from a few hours in the fatal cases to one or occasionally a couple of days. Relapses are frequent, setting in after complete defervescence has occurred.

Prognosis. — "Taking one type of heat-stroke with another," says Dr. Manson, "the case mortality among English troops in India is about one in four." The highest death-rate is to be found among cases of siriasis. Most attacks of heat exhaustion or syncope recover, if treatment be applied. The asphyxial variety of the latter is certainly more fatal.

Sequelæ. — Although recovery from a severe attack may take place, it is commonly the case that the patient's health continues more or less impaired, and often for a long time. Various nervous diseases, such as headache, sometimes severe and persistent epileptic seizures, and even insanity with suicidal or homicidal tendency or mania have been known to follow sun-stroke, and loss of memory, insomnia, and generally deteriorated mental power are frequent. A remarkable intolerance of heat is commonly exhibited by individuals who have once been attacked (see *Jl. Tropical Med.*, Nov. 1898).

Post-mortem appearances. — These may be of the slightest and are rarely distinctive. The temperature may continue to rise after death. Rigor mortis supervenes soon, lasts but a short time, and putrefaction rapidly follows. The blood remains fluid, is acid in reaction, and clots but little; considerable post-mortem staining of the skin and other tissues is to be seen, and extreme engorgement of the viscera, especially the lungs and whole venous system, with sanguineous effusions into the venous cavities. A marked rigidity of the ventricles is described as existing for a short time after death. The substance of the brain and spinal cord is not unduly congested, but the ganglion cells are said to exhibit an acute parenchymatous

degeneration; the meninges are usually hyperæmic and appearances of commencing meningitis have been noted. The liver and renal cells show granular degeneration.

Pathology. — The pathology of these conditions is uncertain, as indeed is the explanation of the regulation of the normal body temperature. A consideration of the symptoms would suggest that the extreme heat, especially that of the sun, by which the most severe cases are caused, exerts an injurious influence on the temperature-controlling centres, whether these be "spinal" or those which regulate the loss of heat, viz. the vaso-motor and respiratory centres, and those which govern the tissues generally, more particularly the muscles, by which the heat is produced. But there is no knowledge how such assumed influence acts.

An explanation of another kind has been proposed for those cases marked by hyperpyrexia. Their suddenness of onset and the general character of their course and symptoms, as well as the apparent occurrence of siriasis in epidemics, and the marked tolerance that is exhibited by the natives and old residents in tropical climates, are features that bear a close resemblance to those manifested by the acute specific diseases, and Dr. Sambon does not hesitate to include siriasis among the infectious fevers. It may be further observed that it is by no means necessarily in the hottest times of the day, nor in the direct solar rays, but rather at night, that the majority of cases occur. Nor is it equally prevalent in all hot countries, for, according to Dr. Sambon, siriasis is restricted to low-lying, sea-coast districts and certain river valleys, and is never met with much above an altitude of 600 feet — in short, that it is an endemic disease dependent upon extreme heat for its development, but not owing its causation to that condition.

Treatment. — Much may be done in the way of prevention by the observance of certain precautions, especially by new-comers in those regions where the liability to attack is greatest. Avoidance of exposure to the sun and protection of the head and neck by suitable coverings are essential, and scarcely less so are light, loose, woollen clothing, and free ventilation of the dwelling-rooms, particularly at night. The mode of living should be moderate in all respects — a light diet, a minimum of alcohol, and no excess of bodily or mental labour, but, if possible, a midday rest is most desirable, as well as the encouragement of free skin action by cold baths and simple drinks.

Success in the treatment of the attack largely depends on promptness of administration. For the syncopal and asphyxial forms

stimulants must be given at once and freely by the mouth or rectum, or by subcutaneous injections of brandy, ether or strychnine, as well as sinapisms to the neck or calves. The patient should be kept in the recumbent position and carefully watched for several hours, as there exists a tendency to relapse even in the milder cases. It may be necessary to apply hot bottles or even a hot bath when the surface is very cold.

Inasmuch as one great danger in the hyperpyrexial attack is failure of the heart, stimulation in these cases is equally necessary, but a valuable and all-important adjunct is the application of cold by affusion, sponging, ice packing and cradling, ice-water enemata or cold baths, by which the temperature of the patient may be reduced. The various antipyretic drugs, owing to their depressing action on the heart, are contra-indicated. It is seldom that bleeding is permissible, though it may be beneficial in the asphyxial forms. Subcutaneous injections of hydrochlorate of quinine (gr. v.), or of tincture of digitalis (m. xl.), are recommended by Dr. Manson, but strychnine should not be given owing to the liability to convulsive seizures.

For a person who has experienced an attack of siriasis removal to a temperate climate is imperative, and abstinence from alcohol most desirable. Counter-irritation by blisters to the nape of the neck may be necessary, and benefit follows a course of iodide of potassium or sodium combined with bromides.

The effects of the solar rays or of great heat upon the skin, such as sunburn, freckles, various forms of erythema, prickly heat, etc., will be referred to elsewhere.

(*b*) Cold. — As an etiological factor of disease this has long been recognised, but it is certain that it is not of the importance as a cause that was formerly held — even as a contributory circumstance its influence has been probably over-estimated. It would seem that exposure to an unduly low temperature can rarely be held solely responsible for any special disease, although by diminishing the resistance of the body to microbic invasion, and perhaps of favouring the occurrence of inflammation by vascular disturbance, it may indirectly become an exciting cause, largely influenced by the age, sex, and general condition of the patient. Certain symptoms of disease, however, such as pain, are very liable to increasingly manifest themselves on exposure to cold, especially if this be associated with dampness. Even the local affection known as chilblain appears to depend as much for its occurrence upon the state of the individual

as upon cold, but frostbite may fairly be attributed only to this cause, which may also directly lead to death.

The general effect of extreme cold, according to the degree and duration of exposure, is to repress the vitality until death occurs from coma, or heart failure, or from shock. Previous to this there is successively to be noted, first, a lividity, and then a pallor and wrinkling of the skin, with a feeling of cold and numbness and shivering. The muscular and mental powers gradually fail, the former interrupted by twitchings and even tetanic spasms; a deepening feeling of languor and loss of sensibility, as the senses become dull and the mind cloudy, with a desire for sleep or, as is sometimes the case, a painful wakefulness. As consciousness is lost the sufferer may roar and shout in his delirium, finally, with a failing heart and slowed breathing, to subside into a state of coma which passes into death. An overpowering desire to relieve an intense thirst by eating snow is often a marked and grave symptom of the earlier stages.

Frostbite is a form of gangrene affecting the extremities, chiefly the fingers, toes, ears, and nose, following on exposure to severe cold, and characterised by a progressive redness of the part with increased sensibility and tingling, followed by a change to a bluish or purple colour, and anæsthesia, which becomes more and more intense as the colour is lost; the tissues later becoming white, hard and bloodless, and, finally, black and shrunken, presenting all the appearances of dry gangrene. According to the degree and duration of the cold, so may any of these stages be reached, and recovery take place with more or less loss of structure and impaired function.

The local **treatment** of such a condition consists in endeavouring to restore the circulation by the very gradual application of warmth and by friction of the affected part, which, if it have become gangrenous, should be allowed to separate spontaneously. The general condition of the patient may require attention.

2. Atmospheric Pressure

Owing to the practical impossibility of isolating the effects of atmospheric pressure, within such ranges of variations as are met with at the sea-level or usually inhabited regions, from the other atmospheric and climatic factors, its causal influence on diseases cannot be affirmed. Nor can it be solely held responsible with certainty for the development of symptoms, such as pain, occurring in the course of already existing disease; corresponding in this

respect to the influence of cold, damp, etc. Its importance as a determinant of hæmorrhage has been much overstated; carefully conducted observations going far to prove the contrary. With extremes of pressure, however, such as man is not ordinarily exposed to, there are associated very constant symptoms sufficient to constitute distinct diseases, for which the pressure itself may be properly regarded as the exciting cause, just as definite morbid states are connected with extremes of heat or cold.

The fluctuations of barometric pressure to which human beings are commonly subjected range between 28 and 31 inches; this, in round numbers, would give a pressure of about 15 lbs. in the square inch, or, on the whole surface of the body of an adult man, upwards of 11 tons, of which the individual is ordinarily insensible owing to the pressure being equally exerted in all directions.

The effects that result from raising or lowering the atmospheric pressure are of chemical, not mechanical, origin, and the individual succumbs to a species of intoxication. The partial pressure of the oxygen is the one factor of supreme importance, and, in this condition, whether it be excessive or deficient, the processes of combustion in the tissues are no longer carried to their final end.

(*a*) Increased atmospheric pressure — caisson disease. — Exposure to much increased atmospheric pressure occurs in mines, sinking wells, in diving bells, and more particularly in caissons which are employed for subaqueous tunnelling where the inrushing water is kept back by compressed air. In the latter situation work is sometimes carried on in a pressure of 50 to 60 inches, *i.e.* three to four atmospheres. A pressure above five atmospheres cannot be tolerated with safety. According to Paul Bert all life is destroyed by an air-pressure of twenty atmospheres. Exposed to this vertebrates die in convulsions; insects become paralysed; vegetables shrink up; grains stop germinating; bacteria cease to ferment. An atmosphere containing either an oxygen tension of 400 mm. of mercury or a carbon dioxide tension of 30 mm. is absolutely irrespirable. The physiological effects, or those which can scarcely be termed disease symptoms, are briefly a general sense of comfort with distinct increase of muscular power, which is exerted with less fatigue; the compression of the gases in the stomach and intestines permits a greater descent of the diaphragm, whereby the respirations become fuller and slower; the pulse is less frequent and of increased volume and higher tension; the blood is less venous and contains a greater percentage of oxygen and nitrogen than normal; and the secretions from the skin and kidneys are increased. Opinions differ

as to whether there is an increase in the tissue metabolism, although the appetite is improved and muscular power increased; for though there may be a slight rise of temperature, it is not constant nor is there any appreciable excess in the carbonic acid or urinary solids excreted. Since it is the needs of the tissues themselves which determine their metabolism, and the amount of oxygen in the blood at normal pressure exceeds what is required, it is probable that there is no constant increase in the tissue change, and consequently none in the waste products.

The incidence of morbid symptoms among workers in compressed air is very variable, but appears to be largely conditioned by the degree of pressure, the duration of stay in the altered atmosphere, and the completeness of ventilation, the last named being, according to Dr. Snell (*Compressed Air Illness*, by E. H. Snell, M.D., 1896, with complete bibliography), of the utmost importance, whilst he relegates to a position of subsidiary importance the rapidity with which the worker passes from the one atmosphere to the other, which has been generally regarded as a dominant factor in the causation of caisson illness. Among predisposing causes are age, the older men being more prone, specially if there be signs of degeneration, alcoholism, and previous want of food, whilst those taking exertion immediately after leaving the compressed air appear more liable to become ill. The immunity of certain divers and caisson workers to decompression is noteworthy. This may depend on greater elasticity and width of the capillaries, but more probably on differences in the gaseous absorption in different individuals. On experimental grounds there are reasons to think that this is controlled by some compensating mechanism.

Symptoms.—These occur almost entirely *after* the individual has left the compressed air, coming on in from a few minutes to an hour or more, seldom beyond twelve. The most frequent are pains in the limbs or back, especially about the knees, of all degrees of severity, even to being excruciating, sharp, dull, or aching in character, often paroxysmal, and sometimes accompanied by tenderness and swelling. They may be the only symptoms, and usually subside in a few hours, or may be days, seldom lasting longer. In a variable proportion of cases epigastric pain, either alone or with the foregoing, is met with, occasionally accompanied with nausea or vomiting. A remarkable and sudden form of paralysis with anæsthesia sometimes occurs, generally taking the form of paraplegia, more rarely a monoplegia. This may or may not co-exist with the pains described;

sometimes it is spastic in character, sometimes tabetic, with permanent exaggeration of the reflexes; the bladder and rectum are frequently involved, and cystitis has been known to supervene. Auditory vertigo, sometimes with deafness of one or both ears, or tinnitus, and in severe cases with a tendency to fall towards the deaf side, has been noticed. Among other symptoms of variable frequency are a marked pallor of the skin, sometimes with mottling or even ecchymoses, cold sweats, formication, deafness, headache, diplopia, epistaxis, hæmoptysis, and a peculiar dysphagia and feeling of obstruction in the gullet. If the entrance to the compressed air chamber be sudden, and especially if there be any catarrhal or other blocking of the Eustachian canal and passages leading from the frontal, nasal, and other sinuses, then severe pain in the ear or across the forehead may be experienced until an equilibrium of pressure is established; occasionally even the membrana tympani is ruptured. As a rule, complete recovery takes place from all of these symptoms in the course of a few hours or days; sometimes, however, it may be weeks before the patient is quite well, and neuralgic pains have been known to persist for longer. Now and then, in a very variable proportion, death occurs very shortly after passing into the normal atmosphere; unconsciousness deepening into fatal coma is the usual course. Death may be postponed for many days or weeks, and in such cases the patient exhibits the symptoms of acute myelitis.

Post-mortem appearances.—Extreme congestion of the brain, cord, and meninges, as well as other viscera is the most constant; occasionally hæmorrhages in the arachnoid space have been met with, and sometimes the appearances of myelitis, with small rents in the substance of the cord suggestive of tearing, as by escaping gas.

Pathology.—This is undoubtedly obscure, the theories that the condition is due to congestion of the brain and spinal cord from pressure on the surface, or to carbonic-acid poisoning, are inadequate, if not absolutely incorrect. The most reasonable hypothesis is that in the escape of bubbles of gas from the blood on the removal of the pressure, temporary emboli of the smaller vessels are found, causing transient or more permanent damage of the nervous tissues, the latter probably due to lacerations caused by the forcible escape of the gas. In some measure the ill effects are due, certainly in animals submitted to pressures exceeding five atmospheres, to intoxication from the results of perverted tissue metabolism.

Treatment.—Since most cases quickly recover, active treatment is seldom called for. Recompression by placing the patient

in a suitable chamber where the atmospheric pressure may be increased, and *slowly* reducing the pressure to normal, is most effective. Morphia may be required for the pains, or anodyne applications to the affected parts. Some success has been said to follow the administration of ergot, given to cause contraction of the arterioles and so relieve the congestion. For the paralytic symptoms counter-irritation along the dorso-lumbar region of the spine, with strychnine internally, should be employed. It is to prevention, by observance of the precautions indicated, that attention should be specially directed.

(*b*) Diminished atmospheric pressure—mountain sickness. —An extremely rarified atmosphere, such as is met with on the highest mountains, or in balloon ascents, causes well-marked symptoms of a serious character. Differences exist—determined in great measure by the "condition" and fitness of the individual, and the degree of his "vital capacity"—as to the power of resisting a much diminished pressure; but at a height of 16,000 feet and upwards, *i.e.* at about half the normal pressure, certain symptoms are manifested by all. The greatest heights attained have been 23,000 feet in the Himalayas, and 10,000 feet beyond that, or upwards of 6 miles, in a balloon. At such altitudes as these the coincident effect of the great cold has to be considered, and it is impossible to separate the influence of this factor from that of the low barometer. Life is absolutely impossible when the partial pressure of oxygen falls from the normal (160 mm. Hg.) to 40-50 mm. Hg.; but the individual is incapable of muscular activity at an oxygen pressure considerably higher than this. The greater the rate of tissue metabolism the less will be the power of resistance to diminution of pressure; hence the higher the body temperature, or the lower the surrounding temperature, or the more the amount of associated muscular effort, the greater will be the metabolism, and the sooner will the individual experience symptoms of distress. Thus it is that mountain climbers as a rule commence to suffer at lower levels than do æronauts. The greater cold, however, to which the latter are exposed at extreme heights, as well as the greater rapidity with which those altitudes are reached, contribute in an important degree to the severity of the symptoms experienced.

The principal **symptoms** are connected with the cardio-respiratory functions, accompanied by extreme lassitude and fatigue, both muscular and mental. The exhaustion is remarkable; it often supervenes suddenly—as, indeed, do most of the symptoms—and increases as the person ascends, until there is absolute inability to move, or

make the slightest effort. After a brief rest progress may be resumed, soon again to come to a standstill; and this may be repeated until further advance becomes impossible. There may be pains in the muscles of the limbs, and the looseness of the hip-joint from lessened atmospheric pressure has been partly credited with the weakness of the legs. The essential fact, however, is the diminished oxygen tension in the blood, the imperfect removal of the carbonic acid therefrom, and the coincident impaired metabolism, upon which, probably, all the symptoms manifested more or less directly depend. This is especially so in respect to the quickened, shallow breathing, which becomes gasping and difficult, and finally the mouth is kept widely open to facilitate inspiration. The desire for air is insatiable. Sometimes, during the rapid sequence of the respirations, an oppressive pause occurs, and then there arises a terrible feeling of suffocation. The pulse is accelerated and soft; there is palpitation and liability to syncope, and the individual experiences a throbbing of the vessels, particularly in the head. This condition of the circulation leads to vertigo, headache, and, in extreme cases, to unconsciousness. The skin generally is pale and rugose, whilst the face is cyanotic; the perspiration is suppressed, and secretion of urine diminished; the body temperature falls, and there may be bleeding from the gums and nose. These hæmorrhages are due to venous congestion, which results from vaso-motor paralysis and cardiac debility, and these in their turn are primarily due to want of oxygen. The appetite is lost; but an intense thirst is complained of, apparently connected with the parched state of the throat. Nausea and vomiting are by no means constant in occurrence, as the name of the malady might imply. A feeling of constriction at the epigastrium has been noticed, and also deafness and earache from outward bulging of the tympanic membrane. Except at extreme heights, individuals become acclimatised in time to the atmospheric conditions, and experience little or no discomfort. The natives of Thibet maintain an active and vigorous existence at an altitude of 16,000 feet. The co-efficient of absorption of the blood gases is, no doubt, the factor of the greatest importance in regard to this immunity, in connection with which it may be mentioned that the number of red corpuscles is increased in animals kept after long periods at greatly diminished atmospheric pressure.

There are no records of diminished atmospheric pressure causing the death of human beings; but experimentally it is found that the paralysis deepens, and fatal coma ensues, thus differing considerably from death by asphyxia, which occurs in convulsions. Cadaveric

rigidity is said to supervene at once, and to be extreme, which also does not correspond to asphyxial death.

Those exposed to these conditions should dress warmly and lightly, spare themselves as much muscular effort as possible, and, when practicable, take with them a vessel of oxygen gas, by the inhalation of which the symptoms are immediately, though temporarily, relieved.

3. Electricity.

Lightning stroke.—Nothing is known of the influence on health, whether favourable or the reverse, of the ordinary states of atmospheric electricity. The passage of a powerful current through the body is commonly fatal either at once or after an interval of a few hours or even days; or it may determine symptoms of a transient or of a permanent character.

The **symptoms** exhibited by those who do not succumb at once are those of more or less severe shock, or of cerebral concussion. There is insensibility, with a small, scarcely perceptible pulse, and slowed, deep respiration, not always regular; the skin is cool, and the body temperature depressed, and the pupils are dilated. A peculiar expiratory cry has been sometimes remarked, not apparently of pain or consciously uttered, but connected with the disturbance of respiration, caused by the electric shock. The patient may slowly recover in a few hours, or it may be a longer time, though death has been known to follow several days later, even after considerable improvement. When consciousness returns, attacks of intense pain are sometimes complained of, not so much in the neighbourhood of any wound, but in the wrists, or more often in the abdomen and loins. Twitchings of the facial muscles, with extreme loss of power and anæsthesia in the limbs, impaired articulation, deafness or noises in the ears, defects of vision, and hæmorrhages from nose, ears, and mouth, and suppression of urine, are symptoms which occur in varying frequency and degree, and may all be quickly recovered from. Sometimes, however, more lasting effects result, continuing from the onset or arising much later; among these are paralysis, hemiplegia and paraplegia, neuralgia, blindness or other defects of sight, loss of taste and smell, or of hearing, impaired memory and mental power, and even insanity.

Various theories have been put forward as the **cause of death**. Some have considered that the resistance of the tissues to the current has determined a rise of temperature which is fatal, and though anything like a general charring of the body is unknown,

there is usually some local evidence of burning or scorching, and a sufficient rise of body heat might be induced to cause death; others have attributed the result to a sudden expansion of the gases of the blood and liberation of free gases from decomposition of the tissues; others again to failure of the respiratory centre; but careful experiments strongly suggest that the main cause is arrest of the heart's action, and that in these cases, when recovery has followed exposure to a discharge sufficient to kill, the current has probably been conducted solely by the external surface of the body rather than by the blood and fluids which it usually traverses, owing to their lower degree of resistance. Recorded cases usually, but not always, show that a few respiratory efforts are made after the heart-beat has ceased, and the same has been observed in experiments on animals with currents of high potential, when sometimes simultaneous cessation of heart's action and respiration have been noted, but arrest of breathing was never found to precede stoppage of the heart. The influence of the current in inhibiting the heart's action is considered by Drs. Oliver and Bolam (*Brit. Med. Journ.* 1898, Jan. 15) to be directly exerted on the organ, and not *viâ* the vagus nerve.

Post-mortem appearances.—These may be exceedingly slight, but generally there are some marks of injury at the point where the current enters the body, and frequently also at the place of exit. These appear as incised or lacerated wounds of the integuments and subjacent tissues reaching even to the underlying bones, which are sometimes fractured; there is frequently a good deal of effused blood, which tends to exhibit undue fluidity; or there may be only an appearance of bruising and no actual wound. The adjacent hairs may be singed, and some burning and slight charring of the integuments, or sometimes a widespread appearance of scorching with streaks and patches of variable size of intense redness, perhaps with blisters. It is seldom that there is any burning of the clothes, which are frequently torn to shreds and stript in part from the body, but it is noteworthy that damage to the garments by no means necessarily corresponds to the situation of the surface lesions. Sometimes remarkable and extensive red or purple dendritic markings are to be seen, and it is probable that the unequal contact and pressure of the clothes has some share in their production. Internally no very constant appearances are recorded; subserous effusions of blood have been described on the viscera, which are sometimes ruptured, especially the liver and brain, and a similar accident has occurred to the tympanum. The lungs are commonly

much congested. Rigor mortis supervenes rapidly, is of very short duration, and is quickly followed by decomposition.

Treatment.—If the slightest evidence of life be apparent artificial respiration should be at once resorted to and continued for at least twenty minutes; life has undoubtedly been thus saved. Stimulants, such as ether or brandy, must be administered hypodermically or by rectal injection. Morphia may be required for the relief of the excruciating pains above described.

W. H. Allchin.

THE INFECTIONS

The infections or specific infective fevers form a group of maladies which result from the introduction into the body by wounds, by the air passages, or by the alimentary tract, of specific bacteria, each specific infection being the result of the action of a special microbe, or its poisons, on certain tissues, or groups of tissues. In many instances, *e.g.* tetanus, typhoid fever, tuberculosis, and diphtheria, the association of cause (the microbe) and effect (the special form of infection) has been so fully and so carefully traced that doubt can no longer exist in the minds of competent observers as to the real cause of each of these diseases.

In recent years our knowledge of the spread of diseases produced by bacteria has been so far modified that some little confusion has arisen in the minds of various writers as to the meaning of the terms "infectious" and "contagious," and now many avoid the use of either of these words, replacing them by the term "infective." Certain of the diseases produced by micro-organisms which are of course infective can scarcely be looked upon as capable of being conveyed from one patient to another except in a very roundabout fashion; it has therefore been suggested that these diseases should be spoken of as "non-transmissible," whilst those which pass readily from patient to patient are "transmissible." Most if not all epidemic diseases are transmissible; so also are some of the endemic diseases, and a few of them, *e.g.* paludism (malaria) may be said to be transmissible not from patient to patient but through an intermediate host. The distinctions that exist in the mode of transmission from patient to patient either directly or indirectly are of great importance, and it is only by a careful study of them that those engaged in the prevention and cure of disease can come to understand them.

In a number of diseases—scarlet fever, measles, smallpox, and others of a similar character—there is *prima facie* evidence that similar causal factors are at work in their production, and on the ground of analogy a very strong case for their microbic nature may be made out, but up to the present no conclusive or experimental evidence in support of this has been obtained, and although these and similar conditions are classed with the infections, it is because of the clinical symptoms and of the special transmissibility of these diseases, and not because of any experimental bacteriological proof.

In connection with this, Koch, for his own guidance and that of others investigating the specific infections, laid down the following postulates, all of which it is necessary shall be fulfilled before it can

be said to be proved that a micro-organism is the primary etiological factor in the production of a disease.

1. The disease must be of well-defined type and invariably accompanied by (*a*) symptoms so characteristic as to constitute a specific malady, (*b*) a micro-organism of constant form and disposed in a constant relation to the fluids or solid tissues of the host. 2. Further, this organism must be present in the special disease and in no other. 3. It must be possible to isolate and cultivate this organism outside the animal body, to obtain pure cultivations of such organism, and 4, by means of inoculation thereof to reproduce the disease with all the symptoms of the original complaint, or at least a sufficient number of them to give it the specific character. 5. In the animal so affected, the same organisms must be demonstrable in the same relation to the tissues as was observed in the original host. In such cases the experimental proof is conclusive.

Characters of the Microbes

Microbes or bacteria are low forms of plants belonging to the group of the schizomycetes or fission fungi. These organisms consist of minute specks from $\frac{1}{25000}$ in. ($= 1\ \mu$) in diameter, or short threads or rods from $1\ \mu$ in diameter and from 1.5 or $2\ \mu$ up to 6 or $8\ \mu$ or more in length, composed of vegetable protoplasm, each usually surrounded by a firmer sheath; in some instances this sheath is composed of a substance resembling cellulose, which in the case of the bacillus tuberculosis has on its outer surface a coating of some fatty acid.

Multiplication and form.—Bacteria usually multiply by a process of fission or direct division; each organism increasing in size and then dividing into two, the process under favourable conditions being repeated at short intervals of twenty minutes or half an hour. The fission may be complete, the mother-organism simply dividing into two separate and distinct daughter-organisms; or the two newly-formed organisms may remain in contact, sometimes with a slight bond of union between them, forming a *diplococcus* or *diplobacillus*. When they undergo further division and the slight bonds still remain, the division going on in one plane only—transversely to the longitudinal axis—there is formed a chain or *streptococcus* or string of round beads like a necklet, or a *streptobacillus* or *streptothrix* like a string of elongated beads. In some cases the rods increase greatly in length without undergoing any marked division into short lengths, and a *leptothrix* or slender thread is formed; or these threads may assume a spiral or screw form, a *spirillum*, this again often subdividing into short curved segments which are known as "comma-shaped" organisms or *vibrios*, *e.g.* Koch's comma bacillus of cholera. Micrococci may be divided into *diplococci* (pairs), *streptococci* (chains), *tetrads* (the result of division in two planes), *sarcinæ* (or packets, the

result of division in three planes, in which the groups are composed of at least eight cells), and *staphylococci* (a mass somewhat like a bunch of grapes). In appropriately-stained specimens there may be seen running out from some of these micro-organisms (B. typhosus, B. tetani, B. choleræ asiaticæ, etc.) lateral or terminal *flagella* or *cilia*, long or short delicate filaments, single or in groups or bundles, some motile and wavy, others rigid and apparently non-motile.

Although in connection with the infections, specific individual forms of bacteria are described, the fact must not be lost sight of that any form met with in the animal tissues may be merely one of a series, a phase in the existence of one of these vegetative micro-organisms. For example, a coccus under certain altered conditions may become elongated into short rods, and these again may, under different conditions, extend into long threads. In the case of the ray fungus—actinomyces—there may be such swelling of the ends of these threads that they form a series of very characteristic club-shaped organisms, often radially arranged. Similarly the diphtheria bacillus may occur as an exceedingly short pointed rod, or it may grow out into long filaments, or again it may develop into a perfect club-shaped organism.

The **structure** of these microbes may be no more complicated than that above described, but in some cases the protoplasm may be granular or it may be divided into segments, as in bacillus diphtheriæ, or there may be seen clear and refractile bodies (spores, resting spores, or seeds) in the substance of the bacillus, as in the B. anthracis, or at one end causing expansion of the rod, as in B. tetani (drumstick bacillus). From these spores, which are more resistant to the action of antiseptics, heat and the numerous other agencies which tend to interfere with vitality than are the bacteria themselves, full-grown or vegetative bacteria may be developed. The question of **spore-formation** is one of special importance, especially in relation to the stamping out of epidemics, as it is by spores that disease germs, such as those of anthrax, are able to continue their existence under unfavourable conditions. For example, most non-spore-bearing micro-organisms when dried rapidly lose their vitality; the cholera bacillus, the typhoid bacillus and others succumbing, sometimes in a few hours. Organisms, on the other hand, in which spores are developed may be dried, treated with chemical reagents, frozen, heated almost up to boiling-point, and still afford evidence by their germination that they have retained their vitality. The bacillus anthracis offers an example of the importance of a knowledge of this matter. When confined to the blood and lymph spaces in the tissues of its host it develops no spores, and if the animal be buried with unbroken skin and before the discharges from the body come in contact with the air, the bacillus dies out, killed by the organisms of decomposition. Should the bacilli, however, gain access to the air, spores which resist the action of putrefactive organisms, and which may remain a source of infection for some time after the

diseased carcase has been buried, are very rapidly formed. Splashes of blood or of discharges containing spores represent foci from which the disease may spread, especially in farm-yards, where there is plenty of organic material on which the anthrax bacilli can flourish; manure-heaps and margins of ponds under these conditions offering specially dangerous centres of infection. For similar reasons the spores of the tetanus bacillus and the bacillus of malignant œdema are also constant sources of danger in any soil to which they gain access.

Parasitism.—Most micro-organisms that are capable of producing an infective disease are parasitic; they live, multiply, and carry on their vital activities within the body of a living animal host; they are not always easily cultivated outside the body, and certain of them (*e.g.* those producing leprosy and relapsing fever) have not yet been so cultivated. These latter are spoken of as "*obligate*" *parasites*. "*Facultative*" *parasites* are those which, though usually found outside the body, are also capable of leading a parasitic existence in an animal host, then usually giving rise to definite pathological conditions. A *saprophytic* micro-organism is capable of growing on dead organic matter, animal or vegetable. These saprophytic organisms may become parasitic, and some of them, such as the anthrax bacillus, tetanus bacillus, and bacillus of malignant œdema, may lead parasitic and saprophytic lives alternately.

Although the line of demarcation is never absolute, obligate parasites are usually confined to certain localities where the conditions are such that they can be transmitted directly from individual to individual, whilst the facultative parasites which are able to exist saprophytically (as in the case of the diphtheria bacillus or the typhoid bacillus, which may live in milk and other food substances) are exceedingly dangerous to the health of the community, as are also those which form spores, and are thus capable of continuing their species under unfavourable conditions. It is certainly far more difficult to get rid of them than of the more easily killed non-spore-bearing micro-organisms (such as the cholera bacilli) which can live only under very definite conditions.

Pathogenetic bacteria exhibit various degrees of parasitism, but it may be accepted generally that even the most parasitic have little power of remaining active in perfectly healthy tissues. Certain of them appear to alternate between a saprophytic and a parasitic existence (bacillus choleræ asiaticæ, streptococcus pyogenes, and bacillus coli communis), and during these two phases they exhibit markedly different characteristics which sometimes render it difficult to realise that the differences are not something more than merely variational. If cholera bacilli be examined directly they come from a patient who has succumbed to cholera, it is found that they have, in a high degree, the power of producing very active toxins from albuminous substances. If, now, the conditions be even slightly altered, or comparatively weak solutions of antiseptics be added, the bacilli lose their power of resistance and are

easily killed, although the activity with which they performed their work under favourable conditions appeared to be very great. If these organisms be cultivated outside the body for a prolonged period they soon lose some of their characteristic features. They still grow rapidly but do not liquefy gelatine at the same rate as they do in their first few generations after being taken from the patient. They appear to have become more distinctly ærobic in character and to have lost some of their power of producing large quantities of active toxic substances, but on the other hand they have become much more resistant to the action of antiseptic substances, heat, cold, malnutrition, and the like. They have indeed assumed saprophytic characters, and in so doing have become more resistant to external influences. Although they are now less virulent they are more dangerous to the community, from the fact that they are not nearly so readily got rid of, and are therefore enabled to lie fallow and to await an opportunity of attacking proteid material in a fresh host, and, in their new surroundings, of regaining their more virulent characters and toxin-producing powers. Here then is an organism which in the parasitic stage is active but is readily killed, whilst in the saprophytic stage it is far more resistant but not so active as a disease-producer. It is, for this reason, necessary to deal with such an organism as soon as possible after it comes from the body, as it is during this very active phase that it is least able to defend itself. What applies in the case of the cholera bacillus applies directly to all those organisms which have the power of setting up disease whether they form spores or not, and the fact must never be lost sight of that, although pathogenetic organisms appear to become less virulent, their greater resisting power renders them far more dangerous in the production of epidemics than are the more active but less resistant forms.

Cultivation and results.—Such micro-organisms as have been studied at all carefully can be cultivated on sterile media of appropriate nature, broth, peptone-gelatine, agar-agar, solidified blood serum, milk, etc.; it has thus been determined that they have certain definite requirements in the way of food, moisture, and temperature, and only when these are complied with can they do their special work. All require oxygen, hydrogen, carbon, nitrogen, and inorganic salts, especially those of lime and potassium. Unlike the higher plants they are unable to assimilate carbon dioxide, which, however, they produce in considerable quantities. Some of them, the obligatory "anærobes," or those which live only in the absence of air, have the power of extracting their carbon and oxygen from starch, sugars, organic acids, and the glycerines. In rare instances they can derive them only from proteid substances. Others, the obligatory "ærobes," can only obtain the bulk of their oxygen from the atmosphere, whilst a third class, the facultative anærobes, or ærobes, as the case may be, may live under either set of conditions. The more distinctly parasitic an organism is the more necessary it

appears to be that it should have proteid material from which to derive the elements of its nourishment.

When micro-organisms are cultivated in suitable nutrient media and grown *en masse* it is possible to determine some of their specific functions. Certain of them produce colouring matter through the agency of an oxydase or colour-producing enzyme or ferment: a blood red as in the case of the bacillus prodigiosus, a magenta by the magenta micrococcus, a violet by the bacillus violaceus, a smoky blue by the bacillus pyocyaneus, and other pigments by other organisms. Some of these *chromogenetic bacteria* have, in common with others, the power of *liquefying a gelatine medium*, and it is supposed that they do this through the agency of a peptonising ferment, which, in the case of the pus-producing organisms, is a most important factor in the liquefaction of devitalised tissues. The anthrax bacillus, especially when highly parasitic, exerts a similar action on gelatine. Acids—lactic acid, etc., ethers, alcohols and other volatile substances, sulphuretted hydrogen, carbon dioxide, ammonia, may all be produced by bacteria, as also may small quantities of antiseptic substances, methylamines, and the like. Beyerinck describes organisms which have the power of producing a phosphorescent glow—the energy that they derive from their food in this instance assuming the form of light.

Bacteria which are the cause of specific infective disease require for their nutrition much the same elements as do other bacteria, but it is a noteworthy fact that most of them require a larger proportion of proteid, especially albumoses or peptones, than do non-pathogenetic forms, especially for the production of toxic substances, the cholera bacillus, again taking it as an example, being most active in producing its toxic substances when it is supplied with a certain proportion of comparatively crude albumen. It is for this reason apparently that the pathogenetic organisms undergo modifications as to their toxin-forming and pathogenetic activity when they are taken from the body and are compelled to live a more or less saprophytic existence, these activities in some instances, as in the case of streptococci, being multiplied to an enormous extent, by continuous passage through a series of animal hosts. In this way may be explained the rapidly increasing severity of cases at certain stages of epidemic outbreaks of such diseases as scarlatina, typhoid, cholera, and plague.

Toxic products of bacteria.—That exceedingly active soluble poisons are formed by micro-organisms is now fully recognised. Very virulent poisons absolutely separable from the micro-organisms are produced by tetanus and diphtheria bacilli, whilst less active poisons have been obtained from the malignant œdema bacillus. The first of such poisons experimentally produced were those separated from septic matter by Panum and described by him as *sepsins*. At first they were supposed to be substances corresponding to the poisonous vegetable

alkaloids, but now they are known to be derived from much more energetic non-crystalline proteid poisons, which on oxidation into alkaloids, lose much of their virulence. These *toxins* are probably *enzymes or ferments*, separated from the organisms producing them, which, combined with such molecules as globulins, nucleo-albumins, peptones and albumoses, may have very varied characters. The ultimate chemical constitution of these toxins is not yet known.

These amorphous toxic products or proteid poisons may be grouped as follows—(*a*) Those substances which may be looked upon as the direct result of the katabolic processes of the micro-organisms, their secretions or rather their excreted waste-products. (*b*) Those substances, also secreted but still remaining enclosed in the protoplasm, which are built up at the expense of outside materials, and are set free only in very old cultures, or when the bacteria are treated with a very strong alkali or begin to undergo degenerative changes. They may be formed from non-proteid materials, but this is not usually the case. Unlike the enzymes and specific toxins which form the first group, they are extremely resistant to the action of heat, and may even be boiled without their specific properties being altered. When dissolved in alkalis they still retain many of their original properties. When dead bacilli, *e.g.* tubercle bacilli, are introduced into the body the substance locked up in them, when set free, may give rise to the characteristic local degenerative changes. They then *attract leucocytes* by their *chemiotactic* power, and, secondly, through the poisons they contain, bring about degenerative changes and death, not only of the tissues in which they are deposited, but also of the leucocytes that are attracted towards them. (*c*) In addition to these, however, certain substances are the direct result of the re-arrangement of the molecules of the nutrient medium in which the organism is growing, this being usually brought about by the forcible abstraction of certain atoms of the molecule by the micro-organism. (*d*) Moreover, the action of what is known as the saprophytic function of the organism upon the medium itself, as originally constituted, or upon the medium as altered by the micro-organism, may also give rise to certain bye-products. It is evident then that the substances resulting from the action of micro-organisms upon a nutrient medium are not only complex in themselves, but are the result of a series of complex processes which it is often exceedingly difficult to analyse.

Many of the pathogenetic organisms act under very special conditions and upon very complex proteid substances. The results vary greatly, but disintegration of these proteids is never carried so far as in the ordinary processes of decomposition of dead organic matter, animal or vegetable. Consequently substances are formed characteristic of the earlier stages of breaking down, viz. *enzymes* (ferments), *toxins and tox-albumens* (proteid poisons), *albumoses* (partly digested

albumen), *ptomaines* (alkaloidal poisons), and similar substances rather than the simpler nitrogenous or carbon-holding substances of more advanced disintegration—water, carbon-dioxide, ammonia, nitrates, and nitrites, etc. In disease processes we have the results of the action of the products of the earlier stages of decomposition of proteid matter, at which exceedingly complex substances are formed, rather than of the later stages, where decomposition is more fully carried out. By a process of hydrolysis anthrax and diphtheria bacilli and their products convert crude albuminous material into substances nearly allied to albumoses. Hankin and Cartwright Wood maintain that these albumoses, when injected into an animal, exert a protective action each against the specific disease with which it is associated. The enzymes or ferments which appear to precede or to be formed along with the albumoses have in most instances a much greater lethal activity, but they appear to exert a comparatively slight protective effect, although when injected sufficiently carefully they give rise to modifications in the protoplasm of the cells, which are thus rendered more resistant to the action of toxins. The albumoses appear to have a similar power of bringing about a modification of the cell, which enables it to resist the attacks of the toxin without at the same time exerting the powerful toxic influence which the enzymes exhibit. This production of albumoses or some similar substance in disease is therefore of vital importance in the production of immunity. A number of enzymes which in many respects resemble the toxins formed by disease-producing organisms have been described—amylase, invertin; enzymes which split up glucosides, cellulose, urea, and fat; enzymes which have the power of peptonising albuminous substances and converting them into peptones, albumoses, and similar proteid derivatives; chromogenetic enzymes which have the power of producing colouring matter, etc. These enzymes may remain and do their work in the cell, hydrolising the cell substance, or they may become separable functions and do their work outside the cell. It has been argued that the so-called anti-toxin present in the blood serum of a patient recovering from an attack of diphtheria or tetanus is simply the accumulation of such a "separated or separable function" which can act on the toxin outside instead of within the cell. Upon this the theory of the anti-toxic treatment of these diseases, *e.g.* tetanus and diphtheria, may be said to depend. The toxins are exceedingly complex substances, and although they are frequently spoken of as being specific poisons, it must be remembered that they are probably combinations of non-specific substances with perhaps a single specific poison (enzyme *plus* globulin, etc.). In diphtheria and tetanus toxins, for example, there are certain common substances by the action of which fever, general symptoms, or local swelling may be set up, but in addition to these there is in tetanus toxin a specific substance which exerts a selective action on certain nerve cells, inducing the specia

and characteristic symptoms by which tetanus may be distinguished from almost any other disease. In diphtheria toxin too, along with the substances that produce general effects, are those which pick out portions of the nervous system, and, combining with these, or acting upon them, give rise to the paralytic symptoms so often developed during or after an attack of diphtheria. Now it is evident that in the treatment of disease by anti-toxins it is necessary not only to antagonise the specific but also the general actions of these poisons. It is possible to imagine that substances which only exert a specific effect may be produced along with others which attack the general poisons. The specific action is, however, always the more difficult to obtain. It is possible that by the use of a "general" anti-toxic substance a patient might be helped to tide over the effects of the action of the specific toxic substance; and the possibility must be recognised that an anti-toxin for diphtheria, for example, might be of such a character that it would enable the patient to recover, still leaving unaffected the specific action on the nervous system. This, however, is not probable.

It is of course necessary to have this specific "function" as highly developed as possible in all anti-toxins. This can best be effected apparently by first treating the anti-toxin-bearing animal with the albumoses and secondly with the toxins. In the complex tox-albumoses, tox-globulines and tox-peptones it is difficult to make out the exact position of the enzyme-like toxin which has been obtained by Martin, Brieger, Cohn, and others; but there is undoubtedly a substance (not a proteid) which has most of the characteristics of an enzyme (is very susceptible to the action of heat, etc.), except that it has a much more limited action than has an ordinary enzyme, not going on working continuously and hydrolising almost indefinitely. It is produced only by specific micro-organisms, and appears to have the power of acting upon certain forms of albumens and of producing tox-albumens or proteid toxins.

Serum diagnosis.—In addition to the anti-toxic substances present in the blood of immune animals there appears to be one which exerts a peculiar action on the specific microbes associated with the disease for which the immunity has been obtained. This has the power of causing some change in the bacteria, as a result of which they become less motile, and run together to form little clumps. This has been termed an *agglomerating or agglutinating substance*, and was first pointed out in 1889 by Charrin and Roger in connection with the serum from animals immunised against the bacillus pyocyaneus. It was again observed by Metschnikoff in 1891 in connection with the vibrio Metschnikovii; this organism losing its motility and becoming agglutinated into little masses in the presence of serum from animals made immune to the action of the vibrio Metschnikovii. Three years later Pfeiffer pointed out that bacteria introduced into the peritoneal cavity of

immune animals became degenerate and less active, but he insisted that this took place only in the peritoneal cavity. In 1895 Bordet and Max Gruber demonstrated that the same change took place outside the body, and in 1896 Durham extended these observations very considerably. Widal was the first observer to publish records of cases in which it was observed that the agglutinating substances are present in the blood at a very early stage of an attack of the disease. The important point, as first indicated by Gruber, is that as this substance is produced at a very early stage of the disease, the method might be utilised as an early diagnostic method. In the case of typhoid fever, which may be taken as a typical example, it is found that in a certain proportion of cases a dilution of the patient's serum with nine parts of normal saline solution invariably gives the typhoid reaction, *i.e.* actively growing typhoid bacilli become inert, are massed in clumps, sometimes in as short a period as five minutes, though where the amount of agglutinating substance is small complete agglutination may not occur until the end of the second hour, though usually it is seen within the first. Normal serum, *i.e.* serum from patients who have never suffered from typhoid, diluted to this extent may also give the reaction with the typhoid bacillus. A more or less perfect reaction is obtained with this dilution (1 : 10) of typhoid serum with the bacillus enteriditis. With the bacillus coli no reaction is obtained. With more dilute solutions of the serum, 1 to 30, healthy blood gives no reaction; the enteriditis blood may give some reaction, whilst the typhoid reaction is usually obtainable. It is thus evident that these substances have a distinctly specific action, and if the solutions are dilute enough the test is very reliable. This serum diagnosis may be applied to other diseases, but it has found its greatest practical application in typhoid fever.

Resistance of the Tissues

In considering the infections it is necessary to take into consideration two distinct elements: (1) the attacking agency, the micro-organism with its poisons; (2) the mechanism of defence with which every living tissue is provided, by means of which the invasion of the attacking organisms may be repelled. When infection takes place the attacking powers must be strong or the resisting agencies weak, and as one or other of these preponderates so are the organisms killed and infection prevented, or the parasitic organisms prevail, and make good their position in the body. Every surface and cavity of the body is covered with or lined by well-developed epithelial cells, which have the power when in health of resisting the attack of most micro-organisms. It is only when these epithelial surfaces become impaired, and their vitality lowered by the action of irritant material or removed altogether by abrasion, that micro-organisms have any chance of getting beyond the

surface. Of course in partially closed cavities, where enormous numbers of micro-organisms can accumulate and give rise to their specific products, the epithelium may in time become so devitalised by the attacks of the accumulated poisonous products that it can no longer resist the advance of the organisms.

Within the tissues themselves it further appears that there exists a series of natural protective agencies which play a very important rôle in the prevention of infection. For example, the blood plasma (Von Foder) and the blood serum (Nuttall) exert a distinct *microbicidal* or *bactericidal action* upon germs, this action varying apparently with the state of health or special preparation of the individual.

Then again there is the *phagocytic or devouring action of cells*, which, at first supposed to be specific, is now coming to be looked upon as a general destroying and scavenging agency. Phagocytic cells go about the body taking up dead or weakened cells and digesting them after withdrawing them from the circulation. Bacteria, foreign particles, pigment and the like, are also taken up by them and carried from point to point or deposited in places where they can do but little damage. These cells are constantly traversing the blood vessels (in increased numbers in leucocytosis) and lymph channels; they constitute an important protective agency, as it is held that, in addition to the phagocytic action, there exists a distinct bactericidal substance in the oxyphile granules so numerous in certain forms of leucocyte; and certainly the greater the need for them the more do they put themselves in evidence. It is perhaps for this reason that we associate them so directly with processes of disease. When pathogenetic organisms—irritating foreign bodies—have made their way into the tissues, attracted there by organisms or their products of action and interaction upon the fluids and tissues (chemiotaxis), phagocytes immediately engage the advancing organisms. At those points where there is a constant danger of invasion, as at the top of the throat (tonsils) and in the lower part of the intestine (Peyer's patches and solitary glands), accumulations of these cells are met with, which may be looked upon as normal phagocytic structures. In the lymphatic glands in the axilla and groin are similar masses of active cells, which have the power of devouring any foreign particles. When these phagocytic cells are badly nourished or overworked they are no longer able to cope with the invading disease germs as they are when active and well nourished and with every opportunity of getting rid of their effete products. Nourishment, rest, and the removal of effete products have the same influence upon the condition of the individual cells of the body that they have upon the body as a whole; such cells require not only exercise, but food and rest, just as surely as do our brains and muscles, and unless they obtain them, and other favourable conditions are maintained, they cannot perform either their scavenging or protective functions properly, and

they and the individual are laid open to the attacks of pathogenetic germs.

In recent years so much attention has been directed to the connective tissue protective agencies that there may have been some danger of the importance of *the part that various functionally active organs play in the prevention of disease* being overlooked; but remembering the share that the suprarenal body and the thyroid gland, with their secretions, the spleen, the liver, the kidney, the intestine, and the bone marrow, take in the formation of blood, in the elimination of waste products, and in similar operations, one cannot but be struck by the fact that, should any of these have their vitality lowered or their activity impaired, they must necessarily leave the body more open to attack than when they are performing their functions properly. It is therefore necessary to insist not only upon the activity of the disease-producing germs as a causal agent, but also upon the weakness of the tissues, or the functional disturbances of the various organs as powerful predisposing causes. The part that the liver plays in protecting the body not only against ingested poisonous substances, but also against certain of the products of digestion formed in the stomach and alimentary canal (autogenetic poisons), may be instanced as an example. This organ acts as a kind of storehouse not only for food materials but also for toxic substances, retaining them in bulk as it were, and allowing them to pass into the general circulation only in such amount as may easily be eliminated without much damage being done to the organism as a whole. Again, bile has a very marked effect in destroying or neutralising the activity of certain poisons, *e.g.* snake venom, and the state of the bile secretion probably has a distinct influence on the destruction both of poisons and micro-organisms that may be found in the intestines. The secretions of the stomach and the intestines, and even those of the salivary glands exert a germicidal effect on bacteria, so that any alteration brought about in them may readily be a predisposing factor in the production of infective disease. Not only the micro-organisms, then, but also their power of producing poisons, the condition, general health of the patient and his tissues, and the character, normal or abnormal, of the secretions and their power of destroying toxins or the toxin-producing organisms themselves, must all be considered as playing a part in the production of this class of disease.

Immunity.—It has been observed in connection with the incidence of the infections that some individuals are decidedly less susceptible to the attacks of certain of them than are others. It has also been noted that certain races resist the attacks of one disease, but are more liable to the attacks of others. For example, it is said that although a negro of West Africa is comparatively immune to the action of the malaria *materies morbi*, he may be very susceptible to the action of the tubercle bacillus; whilst the Indian, though somewhat less susceptible to typhoid than the Anglo-

Saxon, is much more readily attacked by bubonic plague. Numerous other examples of racial immunity and susceptibility might be given — as, for instance, the extreme susceptibility of the North American Indian to measles and smallpox. As the conditions are not absolutely sharply defined, and as other factors connected with artificial immunity here come into play, it is perhaps well not to insist too strongly upon this special form of insusceptibility. A single attack of certain diseases induces a most marked protection against future attacks, and now that it is possible, by experiment on animals, to produce by the injection of micro-organisms or their products the important and characteristic symptoms of many of these specific infective diseases, we can gatl er and arrange numerous observations on this point, and draw certain deductions from them.

It may be well to point out that there is no such thing as absolute immunity, and that the term is used entirely in a relative sense, as indicating a greater or less degree of insusceptibility to the attacks of certain diseases. The hen, for example, is naturally immune or insusceptible to the attack of the anthrax bacillus, though, when the temperature of the fowl is lowered, it may lose much of this insusceptibility. An acquired immunity is really an insusceptibility induced through the production of antitoxin, through the strengthening of the tissues and their cells, or through a specific modification of the cells, as a result of which they are enabled to carry on their work in the presence of parasitic bacteria and their poisons.

It will be well to take as an example a specific disease for the purpose of illustrating the action of micro-organisms in the production of disease, local and general, and to show how, in the course of such a disease, there is a development of certain qualities and substances in the tissues and in the blood, by means of which the patient is protected against future attacks for longer or shorter periods.

If small fragments of the fresh membrane removed from the fauces of a patient suffering from diphtheria be teased out on a slide, and then pressed out with a cover-glass, and the resulting preparations stained, one in methylene blue and another by Gram's method, there may usually be found in them, on microscopic examination, a number of slightly curved or pointed rod-shaped bacilli, which, in the methylene blue preparation, have transverse markings of light and dark bands. Along with these rods, diphtheria bacilli, which are sometimes clubbed at the ends, and occur singly or in small irregular groups, and are the active specific agents in the production of local and constitutional symptoms of diphtheria, there may also be found a number of rounded or ovoid organisms arranged in clumps or chains, these being seen in greater numbers in the methylene blue than in the Gram-stained specimen. The diphtheria bacillus carried, directly or indirectly, from some other patient to the mucous membrane of the uvula and tonsils, especially when these are ulcerated

or inflamed, produces in the albuminous exudation in and on which it lives and feeds, a series of substances, some of which appear to exert a distinct local necrotic effect; others again produce rise of temperature, etc. That this is not a fanciful description may be proved by direct experiment, as pure cultures of the diphtheria bacillus, grown in peptone broth, with or without crude albumen, are found to contain all these various substances, even after the bacilli have been removed by means of careful filtration. In the majority of cases the diphtheria bacilli are confined strictly to the lesion in the throat, where, however, they form their toxins in such large quantities that, as they are absorbed, the patient exhibits the constitutional symptoms characteristic of diphtheria.

How far-reaching and profound is the action of this toxin may be gathered from the fact that as it is excreted by the kidney it gives rise to cloudy swelling of the epithelium lining the convoluted tubules of that organ. It sets up similar changes in the parenchymatous cells of the liver. In the wall of the heart, especially during the later stages of the disease, the muscle fibres are found to be undergoing a fatty degenerative change, in form similar to that following on cloudy swelling, whilst some of the voluntary nerves and muscles, especially those of delicate structure and that are constantly in use, are undergoing similar changes. In the local lesion it is found that the false membrane usually consists of the epithelial cells of the part embedded in fibrinous lymph, with diphtheria bacilli on and near the surface. The cells undergo a rapid degenerative change known as "coagulation necrosis," this often at some little distance from the diphtheria bacilli on the surface of the false membrane.

In very acute cases terminating fatally, this localisation of the diphtheria bacillus may not be maintained; the toxin breaks down the powers of resistance of the tissues by which the bacillus is kept in check, causing such degeneration of the comparatively resistant cells forming the wall of the minute blood vessels that the blood is allowed to escape from its proper bounds into the surrounding tissues, thus giving rise to what is known as "hæmorrhagic" diphtheria, or diphtheria in which hæmorrhages into the skin and mucous membranes constitute a characteristic feature. If, however, recovery is rapid and the diphtheria bacilli disappear from the throat, the patient usually possesses a certain degree of immunity against a second attack, though such immune condition is of but short duration. During the attack of the disease certain changes have taken place in the tissues, and substances have been produced and have accumulated in the fluids of the body by means of which the action of the toxin produced by the diphtheria bacillus is neutralised. That this protection is the result of the action of substances produced by the diphtheria bacillus upon the tissues of the body we have evidence in the fact that if small quantities of a filtered broth culture of the diphtheria bacillus, or, still better, a culture grown in serum peptone broth, be injected at first in small quantities and then

in gradually increasing doses under the skin of a sheep, rabbit, or horse, care being taken to produce a local swelling and a rise in temperature as the result of each injection, and to make the next injection before the effects of the last has passed off, two things will occur: (1) the tissues of the animal react less and less each time to the same dose or even to increased doses of the toxin; and (2) the blood of the injected animal or the serum separated from it is found to have acquired the property of neutralising the action of the diphtheria toxin when mixed with that substance before it is injected into the subcutaneous tissues of an experimental animal. It appears that this substance, so long as it remains in the body, has the power of protecting an animal against the action of the diphtheria toxin; it is an anti-toxin. More than this, however, it has the power, when mixed with the toxin in a test-tube, of completely neutralising the action of this toxin and of rendering it inert when injected into the body—at any rate so far as its lethal and other obvious noxious properties are concerned. The substance contained in the blood has at present not been obtained as a chemically pure substance, but it is evidently a material of very great potency. Its properties have only been studied by their effects in neutralising toxin—hence the name "anti-toxin." The serum in which it is contained is known as anti-toxic serum. Further, by the introduction of small quantities of this anti-toxic serum, animals may be rendered temporarily insusceptible to the action of the diphtheria poison. They are in fact protected against the disease, and are said to have acquired a degree of "*passive*" *immunity*. This passive (or hæmatogenic) immunity is entirely the result of the presence of an anti-toxic substance, which has been produced in another animal, circulating in the fluids of the body of the new host. It at once seizes upon and neutralises any toxin that may be absorbed from without, which thus never remains uncombined or free to exert its specific action upon the cells of the body, especially those of the nervous system. As soon, however, as the anti-toxin has been neutralised by a sufficient amount of toxin or has been excreted from the body by the various emunctory channels, the animal or patient is no longer protected. This "passive" (Ehrlich) or "anti-toxic" (Behring) immunity may therefore be characterised as of a purely temporary character, unless the serum injected be derived from an animal of the same species as that which is being treated, when, according to Ransom, the immunity is more prolonged.

It is possible, however, to produce in an animal or in a human being an immunity of a much higher order and of a more enduring character. It has already been pointed out that doses of toxin gradually increasing in quantity may be administered to an animal, until enormous doses may be given without producing any very serious effect.. Let a standard lethal dose of diphtheria toxin for a horse be taken as being represented by 1 c.c. of toxin. One of these animals, by first receiving injections of

smaller quantities than 1 c.c., and then of increasingly large doses, may in the course of a comparatively short time be brought to withstand the action not only of 1 c.c. of the toxin but of as much as 500 or 1000 times that quantity. It is found, moreover, that this high degree of immunity may be maintained for a considerable period. Such *immunity* is spoken of as being "*active*" (Ehrlich) or "*isopathic*" (Behring), and the reason for this appears to be that it is due not merely to the presence of anti-toxic substances already present in the body, but to the fact that owing to the continued action of large quantities of toxin upon the tissue cells, these cells have, as the result of a special stimulation, acquired the power of producing, even under ordinary non-specific stimulation, a considerable amount of anti-toxin, so that as that which is in the circulation is neutralised or excreted, fresh supplies are constantly poured in from the cells that have acquired the habit of producing anti-toxin (histogenous immunity). Let us apply what has been proved in the case of diphtheria to the other febrile diseases, to smallpox, scarlet fever, and similar conditions in which an immunity is produced by one attack of the disease, and we have a good working theory as to the causation of disease or of certain of the symptoms and pathological conditions occurring during the course of such disease, and an explanation, as yet more or less imperfect, of the method of production of the resulting immunity. In *vaccination* as a protection against smallpox, "vaccine" or the fluid from *cowpox* vesicles is used as the immunising substance instead of the more virulent smallpox virus. When the living smallpox virus or other virus is introduced or injected under the skin, the disease is said to be *inoculated.*

As already pointed out, in some acute infections a certain degree of protection against any further attacks may be conferred by the first. In typhoid and scarlet fevers, measles and smallpox, the insusceptibility may remain with the patient for a considerable period. On the other hand, in such conditions as influenza, a first attack appears to confer little if any immunity; indeed it appears to be the general experience that the first attack predisposes to a subsequent one, whilst in the case of a number of other diseases, of which diphtheria may be taken as an example, any degree of protection that is usually conferred is very transient.

Predisposition

It may be stated generally that the more powerfully parasitic a micro-organism is, and the more luxuriantly it flourishes in the animal body, the less are any predisposing causes required to bring about infection, but the more rapidly should it be possible to cope with an outbreak of the disease, especially if the disease runs a comparatively rapid course. When the course of a disease is more prolonged, as, for

example, in the case of tuberculosis, the infective material is thrown off in considerable quantities over this prolonged period, and the danger of infection is of course increased. Where a disease-producing organism is more saprophytic in character the danger of infection becomes much greater, especially in those localities in which the disease is endemic; in such a case, however, it will be found that the importance of the question of predisposition becomes enormously increased, and it may fairly be said that if it were possible for residents to maintain a condition of perfect health apart from the endemic disease, that this latter would have very little power of attacking them. It may be said of almost all infective diseases, however, that they have little or no chance of gaining a foothold in the human body unless there be disease of some kind, or weakening of the tissues, or a distinct lesion, in which the organisms may find a nidus and sufficient and suitable nutriment.

It is for the physician to consider carefully what these predisposing causes are, as during an epidemic he may at any time be called upon to advise those under his charge as to the best means of avoiding the prevailing disease. It has been pointed out by Koch, and further emphasised by M'Leod, that a normal healthy guinea-pig is absolutely immune to the attacks of the cholera bacillus. When, however, the acid secretion is neutralised by the introduction of an alkaline fluid into the stomach, and when at the same time the peristaltic action of the intestine is interfered with by the exhibition of morphia, the cholera organism is enabled to run the gauntlet of the stomach, and to multiply in the intestine to such an extent that it can produce a sufficient amount of its toxins to kill the guinea-pig with the utmost certainty. Here there has been produced by artificial means a predisposing condition, the series of natural resistances being for the time removed.

Similarly it has been found that animals kept at a low temperature and on starvation diet become extremely susceptible to the action of certain disease-producing germs; whilst an atmosphere containing sewer gas, or an excessive amount of carbonic-acid gas, and exhaled organic matter, may also predispose to the action, say, of the typhoid germ. Certain rash experimenters, confident of the good condition of their digestive apparatus, have from time to time taken into their stomach cholera and typhoid germs in the form of pills, and the results have been negative; but it is well known unfortunately through a very large number of well-recorded cases, that these same germs when taken in water have produced very definite disease. During an epidemic produced by water-borne cholera or typhoid organisms, it has often been noted that only a proportion of those who have consumed the infected water are affected. All must have received a dose of the bacilli, but all are not attacked by the disease. This difference must undoubtedly be due in part to a difference in the general resisting power of the patient, though in some cases it may be that a specific immunity has been conferred, sometimes

by an attack of the disease, and sometimes imperceptibly through a long-continued exposure to gradually increasing doses of the toxin or specific organic substances. I have obtained direct evidence, for example, that the acid gastric juice exerts a most marked effect in diminishing the activity of the tubercle bacillus and of the cholera bacillus. It has been noted by Metschnikoff that during an epidemic of cholera large numbers of the specific bacilli have been found in the intestines of healthy individuals, and it may be accepted as the outcome of Hueppe and Cartwright Wood's observations that until there is some inflammation of the walls of the intestine, accompanied by the pouring out of an albuminous fluid, such as is contained in serous exudation, no marked multiplication of the cholera organisms and no appreciable quantity of specific toxin is produced in the intestine.

All the early experiments with the products of micro-organisms were carried out for the purpose of obtaining substances which would act as prophylactics—which would prevent disease; and vaccination and inoculations for the production of other immunities were all directed to such prevention. Pasteur's treatment for hydrophobia, however, went far beyond this, and his inoculations were distinctly curative in their action, in so far as the treatment was not begun until the disease had been inoculated by a bite. In the case of the antitoxic sera, however, a still further advance was made; the diphtheria antitoxic serum, for example, being given for the purpose of neutralising diphtheria toxin and of curing the disease in so far that no further damage is done to the tissues. Such serum is secondarily a prophylactic, but up to the present its main use has been the cutting short of active disease.

General Course and Characters of the Infective Diseases

Proceeding to consider the method of production of the specific infective fevers, it may be well to note what takes place when a single germ of yeast, say, is introduced into any fluid which contains the materials necessary for its nutrition. If a suitable temperature be maintained, and no antiseptics are present along with the necessary nutrient substances in the fluid, the germ begins to grow and multiply with great rapidity. It uses up nitrogenous and saccharine matter, the fluid becomes turbid, and alcohol, carbonic-acid gas, and a number of other substances are produced. Other organisms placed under similar conditions produce colouring matter, others aromatic or exceedingly foul-smelling gases; others again give rise to the production of enzymes or ferments and peptonising substances. A single organism being in most instances sufficient to start a growth very soon makes itself manifest, both by its own presence in large numbers and by the character of its products. Exactly the same sequence of events takes place in the human body when disease germs gain access to its tissues. Such

germs, to maintain their position, must be endowed with a certain power of maintaining a parasitic existence. Unlike saprophytic organisms, which, although they may have the power of producing active poisons, are unable to exist in the fluids and tissues of the body, they have the power, especially when the tissues are taken at any disadvantage, of multiplying and of producing their products — sometimes in large quantities—and acute specific fevers, which run a very definite course, are the result. Each fever has its course divided into a series of stages, each one associated with some phase in the action and reaction between the invading micro-organisms and the tissues of the invaded organism.

Between the time at which a patient is exposed to a definite infection and the period at which the disease manifests itself (*stage of invasion*) there is a period known as the *incubation period.* Following this comes the *period of "fever,"* then a period of *lysis* in some cases, of *crisis* in others—*i.e.* gradual or rapid diminution of the fever (*defervescence*), and, lastly, a period of *convalescence.* These periods may be said to correspond generally to the phases through which a fermenting or fermented fluid passes. When the single grain of yeast is added, little or no change may be observed for some considerable time, so in the case of the specific infective fever there may be no marked evidence of any kind that a pathogenetic germ has been able to make good its position in the tissues of the patient, although in both instances the organisms are multiplying rapidly, and may be producing their products in considerable quantities. This is the period of incubation. It is only after these products begin to exert their gross specific effect on the tissues that any symptoms by which a diagnosis can be made appear. The effects produced vary, of course, with the character of the organism, the rapidity of its growth : these determining within certain limits the length of the period of incubation ; the habitat and nature of the poison determining the character of the symptoms. Thus in scarlet fever the organism apparently affects specially the tonsils and pharynx, the skin and the kidneys, perhaps because the organisms invade the patient by the channels in the former parts, and because of the efforts made by the skin and kidneys to excrete the poison. In the case of typhoid fever the micro-organisms appear to affect the lymphoid tissue of the alimentary tract, especially in the lower part of the intestine ; the spleen is also a seat of election in this condition, whilst the skin is only slightly affected.

As would be expected, the initial dose of the poison may exert some influence in determining the length of the incubation period. If only a small amount of the poison be introduced, and this holds good, especially in the case of such a disease as scarlet fever, the period of incubation may be prolonged ; while, on the other hand, if a very large dose be absorbed, the period of incubation may be very short. This is due not entirely to the mere number of organisms introduced affecting the period through which

multiplication must take place to bring the number up to a certain point; the large number introduced, perhaps, along with a certain proportion of their products, act upon the tissues, and render them less resistant, so that the organisms that have found an entrance are enabled to multiply much more rapidly than when the tissues are not so prepared. Of course different organisms multiply and produce symptoms at very different rates. For this reason, and because they form their products in different positions, and in varying quantities, marked differences are observed in the lengths of the incubation periods of different diseases, *e.g.* diphtheria as compared with tuberculosis.

In the really characteristic stages of a disease the symptoms are, as a rule, the result of the changes induced by the action of micro-organisms on the tissues, and of the tissues on the micro-organisms. For instance, rigors, fever, or an apyretic condition, rapid pulse, increased rate of respiration, conjunctival suffusion, dilatation of the pupil, vomiting, headache, muscular pains, and other nervous symptoms, are attributable to the action of certain of the poisons produced by micro-organisms upon the thermogenic, respiratory, vaso-motor, pneumogastric, and other nerve centres. The swelling of glands, pharyngitis, albuminuria, and the cutaneous rashes occurring in certain exanthematous diseases, on the other hand, are due to the reaction of the cells in the glands, kidney, and skin, to certain others of the poisons as they are being excreted. Proliferation and increased vascularity and joint pains result from stimulation of the cells, nerves, and walls of the blood vessels by the toxin, whilst, in such a condition as typhoid fever, the increase of the lymphoid tissue in the enlarged lymphatic glands indicates a similar process of reaction to the specific stimulation of the typhoid poison.

It is to this specific reaction, during the course of the febrile stage, that the patient owes his chance of recovery. When septic organisms or the anthrax bacillus are introduced, if no marked tissue reaction is set up, the patient, whether brute or human, usually succumbs very rapidly to septic or anthrax poisoning; but when local reaction, in the form of swelling, redness, and œdema is marked, and especially where infiltration with leucocytes occurs, the patient usually stands a fair chance of recovery. It seems to be a general law that animal cells, when repeatedly subjected to a not too powerful specific stimulation, have the power, first, of becoming so accustomed to this special stimulation when gradually applied, that they may in time become capable of carrying on their special functions, even in the presence of larger and larger quantities of the stimulating substances; and, second, of producing substances which, separable from the cells, are capable of directly neutralising the action of the special stimulant, *i.e.* a function of the cell which, under ordinary conditions, remains in abeyance, or develops only in a very slight degree, becomes developed to such an extent that it overflows, as it were, from the cells, and takes upon itself the special function of so neutralising the toxin that

the cell itself is enabled to carry on its functions without being in any way hampered by the presence of the toxin. Every evidence of local reaction, then, whether redness or local swelling, affords an indication that this process of "acclimatisation" and anti-toxin production are going on, and it is only as the cell becomes acclimatised to the presence of the toxin and of the micro-organisms, or, as the anti-toxin is developed in sufficient quantities to neutralise the toxin already formed, or being formed, that the patient recovers, or is protected against future attacks of the disease.

In typhoid fever, where there is a gradual increase in the severity of the disease, there is also, when the patient recovers, a gradual diminution in the severity of the disease symptoms, this taking place during the period of "lysis." During the rise of the fever there is a gradual increase in the amount of toxin present, even though the production of anti-toxin and the process of acclimatisation of the cells may commence at a very early stage of the disease. After a certain period the ratio between the formation of toxin and the production of anti-toxin is gradually altered, and during the period of lysis the relative amount of anti-toxin to toxin rises, until ultimately the whole of the toxin is neutralised, and the period of convalescence is then entered upon—the period during which the gradual repair of the damage done to the tissues is commenced. Anti-toxin can neutralise the poison, but it cannot undo the damage already sustained by the tissues—a damage which can only be made good by the reparative action of the tissues themselves. In the case of pneumonia the disease runs its course much more rapidly. The period of invasion and that of fever are both comparatively short; the production of anti-toxin appears to go on very quickly, and recovery is very speedy, by a "crisis" in which there is rapid inversion of the balance between the toxins and the anti-toxins.

It will thus be evident that in ordinary septicæmias — blood poisonings—bacteria make their way from point to point, carried by the blood through the blood vessels, and the symptoms and lesions are essentially those that one would expect to occur under such conditions. The so-called tissue parasites, on the other hand, appear to be unable to exist in the blood stream itself and only when they come to rest in the tissues. In such a condition as typhoid fever, which may be taken as an example, the parasitic organisms are found specially in the adenoid follicles of the intestine, in the neighbouring glands, and also in the spleen, whither they appear to make their way from the intestine by the lymphatics. It is probable that they are not confined entirely to the lymphoid follicles, and that much more widespread tissue changes are set up than are usually demonstrated. Typhoid fever, then, cannot be looked upon as an ordinary septicæmia, though, under certain conditions, the typhoid organisms may flourish in the blood; it then becomes truly septicæmic in character.

The multiplication of the micro-organism, and the formation of its special products, are the real elements that determine the specific character of the disease; and just as specific fermentations and special colour formations occur, and special gases are formed, so specific diseases may be produced in which the tissues and fluids of the patient are, for the time being, converted into nutrient media, in which micro-organisms can grow and produce their special products, these specific products, by their action on the reacting cells and tissues, giving rise to the specific symptoms. The body of the patient differs, however, in one very important respect from any ordinary nutrient medium. The organisms in the artificial nutrient medium grow for a time with very great rapidity, and then by the production of organic acids, phenols, etc., convert this medium into a fluid in which they are incapable of further development. These substances, however, must be present in considerable quantities, and may usually be detected by ordinary chemical examination before the organisms cease to multiply. In the animal body, on the other hand, such substances are not formed in any considerable quantities; or, at any rate, not in quantities sufficiently large to interfere materially with the growth of the organisms. Nevertheless, the organisms no longer thrive, and the toxins they produce are no longer capable of doing any harm. This appears to be due to the fact that the cells have formed antitoxins which do not act directly upon the organisms, as do the products of fermentation, but only upon their toxins, with the result that the micro-organisms, with their poisons neutralised, are at once reduced to the level of mere saprophytes; they are disarmed and fall a prey to the devouring phagocytes, which are constantly on the alert for all "foreign" bodies coming within their sphere of influence. A patient thus recovers from a specific infective fever, and, having suffered from one attack of a specific disease, has acquired against it a marked degree of immunity, which may continue for a very considerable period.

It is well to bear in mind that mixed infections are of somewhat frequent occurrence. Such infections may be coincident, the organisms finding their way to the tissues at the same time and helping one another to produce their special effects; for example, the tetanus organism is much more to be feared in the presence of pyogenetic organisms than it is when acting alone. Then again the diphtheria organism, when aided by the pus-producing organisms, is capable of doing far more damage than it is alone; whilst pus-producing organisms are often enabled to make their way much more readily into the deeper tissues and then to set up a pyæmia, when they are aided by the diphtheria bacillus acting on the mucous membrane or submucous tissue of the throat. The sequelæ of the infective fevers are very frequently the result of a secondary infection. Mixed infections, however, may occur from the very commencement of the disease; the prognosis of such cases is usually much more hopeless than in the case of the simple diseases.

Terminations of the Infective Diseases

It is evident that the acute infective disease must run a rapid course, though that of an exanthematous disease is more rapid than that of a case of acute pulmonary tuberculosis, which latter condition, however, should be looked upon as a chronic disease which runs a comparatively rapid course. Acute diseases may have one of three terminations. If the poison is rapidly excreted and if the degenerative changes brought about by it are not too profound, there may be practically complete recovery. Even when the patient does not succumb, a series of changes which, without bringing about actual death, may so alter the conditions of growth, secretion, and excretion through the intercurrence of such states as chronic interstitial nephritis, catarrhal nephritis, chronic interstitial hepatitis and similar lesions, that the health of the patient is materially interfered with. The nutrition of the muscle of the heart may be so far impaired, as in cases of typhoid fever, diphtheria, influenza, or the peripheral nerves or the nerve centres may have been so altered by the action of the poisonous products of the disease, that the patient may die suddenly from heart failure when he appears to be well on the road to recovery. In the third mode of termination, death may supervene during the height of the fever, the patient succumbing directly to the action of the toxin on the nerve centres, on the secretory glands, or on the tissues generally.

In the chronic infective disease the poison or toxin is as a rule more dilute, acts for a longer period, and appears to affect the connective tissues, especially those associated with excretory epithelial surfaces. It may be accepted generally that the more chronic the disease the less do the epithelial tissues undergo rapid degenerative changes, but the more is fibrous tissue developed at those points at which the poisonous products are being excreted. For example, in syphilis and tuberculosis the formation of fibrous tissue with coincident or subsequent degenerative changes is exceedingly well marked, and is comparable to the fibrosis of lead poisoning and chronic alcoholism. In actinomycosis, where less poison is formed, this tendency to fibrous tissue formation is more distinctly marked, and there is far less tendency to degeneration even than in tubercle.

The elimination of poisonous products from the body appears to take place by much the same channels as the normal effete matters the result of metabolic processes. The diarrhœa that accompanies the exhibition of certain poisons can only be compared to that met with in cholera and typhoid fever as an effort on the part of the intestines to get rid of noxious material. The acute nephrites that occur during the course of scarlet fever and diphtheria are examples of conditions comparable to that observed in mercury poisoning. The skin also appears to play an important part in getting rid of poisonous products. Typhoid bacilli may be found in the urine and in the bile, and it is probable, as

pointed out by Sherrington, that not only the products of micro-organisms, but even the micro-organisms themselves may pass out through "intact" mucous membranes, especially in the case of the acute infections.

Post-mortem Appearances common to the Acute Infections

In almost all the febrile infective conditions, certain general post-mortem appearances in the patient who has succumbed point to the nature of the disease. In most cases, owing to the degenerative changes that occur in the muscle before death, *rigor mortis* is much less perfect and passes off at a much earlier period than in patients who succumb to other diseases. In many of the fevers, especially those of a specific and septic character, the blood is so changed even before death that it does not undergo coagulation, the capillary vessels lose their tonicity, the blood flows through them readily into the dependent parts of the body, and post-mortem lividity is often very marked, the heart and blood vessels and even the skin being blood-stained. In the cases of acute fever resulting from specific infection, the organs are usually in a condition of cloudy swelling ; they are swollen, paler than normal, and exhibit a very characteristic parboiled appearance. The spleen is usually enlarged and pulpy, especially in typhus. The liver and kidneys at the later stages of the disease present, in addition to this, evidence of fatty degeneration, whilst in the former organ distinct necrotic areas of the parenchyma may sometimes be observed. In almost every fever fatty degeneration of the heart of a more or less marked character occurs sometimes during the second week of the affection, and in certain diseases, such as those already mentioned—diphtheria, influenza, typhoid, and also in almost all of the other infective febrile diseases—this is an important clinical fact that is frequently ignored in the treatment of convalescent patients. Cardiac dilatation is an essential feature of acute rheumatism, due in part to the degeneration associated with myocarditis, and also, it would appear, to a specific toxic effect directly affecting the muscles. The muscles usually participate in the general changes of cloudy swelling and fatty degeneration ; in typhoid and more rarely in other fevers, Zenker's hyaline or vitreous degeneration is also met with.

Classification

In recent text-books of medicine the classification of specific infective conditions or "infections" is based not entirely upon the clinical symptoms as in the older works, but partly upon the nature of the etiological factor,—bacteria or their products,—though in only a certain number of these infections has the actual *causa causans* been demonstrated.

Diseases may be *endemic* or *epidemic*. An endemic disease is one

that is constantly found in a region in which the "local" conditions appear to be specially favourable to the continuance of the existence of the organism producing such disease. An epidemic disease is a sudden outbreak, either through the conditions becoming specially favourable for the existence, multiplication, and transmission of the disease-producing organisms or of the introduction of these organisms from the region in which the disease is already endemic. An epidemic outbreak may occur in a locality in which the disease is endemic; it is then due to the development and bringing into action of special predisposing causes, which do not usually exist, the epidemic character of the disease depending greatly upon the facilities offered for its rapid spread amongst a population specially prepared for its inroads.

The following classification of infections is founded partly upon the specific nature of the organisms present, partly upon the symptoms and changes that result from such actions and interactions :—

I. Febrile Infective Diseases with which Micro-organisms have been definitely associated

(A) Acute

Local

- Boil and Carbuncle
- *Erysipelas

} Due to Pyococci

General

- Septicæmia and Pyæmia
- Infective Endocarditis
- *Puerperal Septic Fever
- Gonorrhœal Infection

} Due to Pyococci

- *Typhoid Fever
- Mediterranean Fever
- *Cholera
- Plague
- *Relapsing Fever
- Yellow Fever
- Weil's Disease

- Anthrax
- Tetanus
- *Diphtheria
- Epidemic Pneumonia
- Infective Meningitis
- Influenza
- Glanders (Farcy)

} Due to Specific Organisms

(B) Chronic

- Tuberculosis
- Leprosy
- Mycoses

* These diseases must be notified to the Medical Officer of Health of the District in which the case occurs, according to the provisions of the Infectious Diseases Act, 1889, Sect. 3.

II. Febrile Infective Diseases with which Micro-organisms have not yet been definitely associated

Acute and Chronic

- *Typhus
- Measles
- Rötheln
- *Scarlet Fever
- Acute Rheumatism
- Chicken-pox
- *Smallpox
- Vaccinia (Cattle)
- Mumps
- Whooping Cough

- Dengue
- Beri-Beri
- Epidemic Dropsy
- Oriental Sore
- Verrugas
- Frambœsia

- Syphilis

- Rabies
- Foot and Mouth Disease (Cattle)

- Mixed Infections

III. Febrile Infective Diseases due to Protozoa

- Dysentery
- Malaria
- Hæmoglobinuric Fever
- Kala-azar

* These diseases must be notified to the Medical Officer of Health of the District in which the case occurs, according to the provisions of the Infectious Diseases Act, 1889, Sect. 3.

G. Sims Woodhead.

FEVER

The word fever is employed to designate a certain assemblage of symptoms. These are a rise of the internal temperature of the body (pyrexia), a quickened pulse, rapid respiration, loss of appetite, malaise, furred tongue, scanty, high-coloured urine, often containing a trace of albumen, and, allowance being made for the diet, an excess of urea, constipation, a flushed skin, sweating, headache and delirium. It is by no means necessary that all these symptoms should be present in the same person for us to say he has fever, and in the above list the symptoms are roughly placed in their order of frequency. Pyrexia is, however, constant, and a patient cannot be said to have fever unless it exists. How far the other symptoms are the result of the pyrexia, or the result of the cause of the pyrexia, is at present undetermined, but many are certainly at times merely dependent upon the temperature, and therefore the terms fever and pyrexia are occasionally loosely used as though they were interchangeable; this is inexact and to be deprecated, but as pyrexia is the only constant sign of fever, and has been more studied than any other sign, in describing fever it is the pyrexia to which reference will chiefly be made. In this article the slight rises of temperature which follow exercise and may be considered physiological will not be considered.

The internal temperature of the human body may be taken in the rectum, the vagina, the stream of urine as it issues from the bladder, the axilla or the mouth: the two first situations give the most accurate results. The mean daily rectal temperature of a healthy adult is 98.96° F., that of the stream of urine is 98.56° F., that of the axilla is 98.45° F., and that of the mouth is 98.36° F., and in each of these cases the temperature in health may be half a degree Fahrenheit below the figure given in the early morning, and half a degree above the figure given in the evening between 6 and 7 P.M. It is more important that the temperature should be taken carefully with an accurate thermometer, than that any particular site for observing it should be chosen. Mistakes most readily occur in the mouth from not keeping it shut, not keeping the thermometer under the tongue, and not noticing whether the mouth has been recently locally heated or cooled; and in the axilla from not keeping the thermometer well in position. The groin is an excellent situation for taking the temperature of children. The healthy temperature of different adults differs slightly, but only a fraction of degree, for one of the striking characteristics of the higher warm-blooded animals is the uniformity of the temperature of different adult individuals of the same species. With children this power of maintain-

ing a fixed temperature is not so striking. The fœtus in the early months of intrauterine life is cold-blooded, and it is only gradually that the individual acquires the power of so controlling the balance between loss and production of heat that the temperature is constant. Therefore in children slight causes, which would in an adult be inoperative, may cause considerable pyrexia, perhaps without other signs of fever; even simple constipation may cause the temperature to rise to 104° F. Hence it is that pyrexia is often less alarming in children than in adults.

It is conceivable that the temperature of the body might rise because, other things being equal, its specific heat decreased, but there is no evidence that this ever occurs.

The temperature remains nearly constant in health, because the production of heat which takes place chiefly in the muscles is exactly counterbalanced by the loss which takes place chiefly from the skin by radiation, and by evaporation of sweat, and the fundamental problem in the study of any case of pyrexia is, whether the temperature has risen because the loss of heat has diminished while the production remains the same, or whether the production has increased, the loss being unaltered, or, lastly, whether both production and loss having varied the temperature has risen because the two classes of variations have not counterbalanced each other.

Three chief methods have been employed in attacking this problem, (*a*) the calorimetric; (*b*) the chemical; and (*c*) the clinical; and full accounts of each will be found in my Croonian lectures on "The Means by which the Temperature of the Body is maintained in Health and Disease," 1897. The calorimetric is so complicated and so full of fallacies that it cannot be described here, and the chemical, which has yielded some most important results, is very difficult to apply at the bedside, but its results show that in animals some fevers are certainly accompanied by a considerable increased production of heat. Probably we must be especially cautious in applying to man conclusions about fever arrived at by experiments on animals, for as many of them do not sweat and have thick fur, their loss of heat must differ from that of man. The method which I have called the clinical depends upon the following considerations. It is clear that when the surface temperature of the body rises the loss of heat by radiation and conduction will be increased, and that when the amount of sweat secreted is increased, the loss of heat from evaporation is increased, so that if in any case it can be shown that the internal temperature has risen and at the same time the surface temperature has risen and the amount of sweat secreted has increased, the production of heat must have increased, provided that the temperature of the surrounding air is constant, and in the wards of a hospital it is kept nearly so. The internal temperature is registered with an ordinary accurate clinical thermometer, and the surface temperature is taken with special flat

bulbed thermometers. The sweat is estimated by using calcium chloride as an absorbent. It is fused into the bottom of a glass box which has an air-tight lid; the box and its lid are weighed; the box with its lid off is then inverted at a given spot on the skin for a given time, the lid is at once put on, the box is again weighed, and the gain in weight represents the amount of sweat absorbed. There are many small details to be attended to which I described elsewhere. A series of observations are made on the patient when his temperature is raised, and another series when he is well and his temperature has become normal. A comparison will show whether, when the temperature was raised, the loss of heat by radiation and evaporation was more or less during fever than during health. If it was more the production of heat must have been enormously increased during the febrile period, for not only was the internal temperature raised, but the loss of heat was greater. But if it was less it must have been that some at least of the rise of internal temperature was due to a diminution in the loss of heat. A series of observations carried out by this method showed that in typhoid fever the pyrexia was largely due to a lessened loss of heat, that in pneumonia there is a very considerable increased production of heat, that in erysipelas there is also an increased production of heat, and that in suppuration there is a diminution in the loss of heat. These results show that sometimes the pyrexia of fever is due to an increased production of heat, and that sometimes it is due to a diminution of the loss, that is to say that different toxins produce fever in different ways. This is a different view from that of some older writers, who endeavoured to explain all fever by the same process.

It is interesting to note that typhoid fever, although a long-lasting disease with a high temperature, has a low mortality; the reason for this may be that, as the loss of heat is diminished, the temperature is raised with the least expenditure of energy, and it is also interesting to observe that experience has shown that the best way to reduce pyrexia in typhoid fever is by the external application of cold water, that is by increasing the loss of heat. On the other hand, pneumonia is a disease in which the pyrexia lasts but a little while compared with typhoid fever; as it is due to an increased production of heat the patient could hardly survive a long-continued fever accompanied by such a loss of energy.

Pyrexia occurs clinically either (i.) as a result of disease or damage of the central nervous system, *e.g.* that which follows hæmorrhage into the pons or (ii.) as a result of the introduction of a poison into the body, *e.g.* the pyrexia produced by atropine poisoning or that of the specific fevers in some of which, *e.g.* diphtheria, the toxin which causes the pyrexia has been isolated. Cases often occur, especially in children, in which the only evidence of toxæmia is pyrexia and other febrile symptoms; usually, however, there are other associated phenomena, *e.g.* the rash of scarlet fever, the physical signs of pneumonia, the inflammation of the joints in

rheumatic fever, by which we can distinguish the disease, and sometimes, as in the case of diphtheria, malaria, or tubercle, recognise the micro-organism which, by its power of manufacturing toxins, causes the febrile symptoms.

(i.) That damage to the central nervous system will cause pyrexia has been shown chiefly by experiments upon the corpus striatum and spinal cord. I have published twenty-seven experiments in which the corpus striatum of rabbits was experimentally damaged. The rise of the rectal temperature was sometimes over 4° or 5° F., and the average rise was 2.74° F. This was always after a unilateral lesion, and the pyrexia never lasted more than a day or two.

In clinical medicine lesions in the following positions will cause pyrexia. (Full references will be found in an article in the *Brit. Med. Journal*, Nov. 17, 1894.)

(A) *Cortex.*—Dr. J. H. Bryant has shown that out of a hundred cases of hyperpyrexia (*i.e.* temperature over 106° F.), in eight it was due to injury of the cerebral cortex. Usually there was also meningeal hæmorrhage, but in one there was only laceration of the cortex. The temperatures were 109°, 108.4°, 107.8°, 107.4°, 107°, 107°, 107°, and 106.6°, and it is by no means uncommon to meet with pyrexia after lesions of the cortex.

(B) *Corpus striatum.* — So many cases have been referred to by myself and others, that it is now known that hæmorrhage into the corpus striatum is frequently followed by pyrexia, unless the excessive loss of blood keeps the temperature down. The rise may be as high as 108° F. If only one corpus striatum is damaged the rise of temperature is often higher in the axilla of the paralysed limb, that is to say the one opposite the lesion, than in that on the sound side. By comparing the variations in the loss of heat on the two sides of the body I have been able to show that the loss is greater on the paralysed side; therefore, as the axillary internal temperature is raised on this side, it follows that the production of heat is increased on the paralysed side, so that in this form at least of cerebral pyrexia the production of heat is increased. The usual course of the axillary temperature after an ordinary cerebral hæmorrhage implicating the corpus striatum is that for the first few hours there may be a fall below normal, owing to the shock and loss of blood, but as the effects of this pass off the rise shows itself. The maximum is usually reached within twenty-four hours. The temperature then slowly falls, the normal point being reached in a few days. After this it generally falls a degree or so below normal, and remains subnormal for a few days before attaining the healthy standard. When it is subnormal it is still a little higher on the side opposite to a unilateral lesion. Other lesions of the corpus striatum will produce pyrexia.

(C) *Crura.*—Lesions of these may cause a rise of temperature; for instance a case is recorded in which a tumour pressed on the crus, and a temperature of 107.4° was reached.

(D) *Pons*—(E) *Spinal cord.*—It is so well known that damage to these structures will cause pyrexia that it is hardly necessary to quote cases.

Therefore it appears that fibres proceed from the cerebrum, probably the corpora striata, and pass down by way of the crura, pons and cord to the muscles to influence their thermogenetic function. The cortex too clearly has some influence; how it acts we hardly know; it may be that it influences the corpus striatum, or that there are thermic fibres proceeding directly from the cortex. It must be remembered that the mechanism by which heat is lost is also under the control of the central nervous system, but the observations just quoted upon the temperature in hemiplegia, the absence of any visible diminution in the radiating and evaporating power of the skin even in some cases of hyperpyrexia, and the very suddenness and great extent of the rise in some cases of damage to the central nervous system all point to the fact that, in some cases at least, the pyrexia that follows it is due to an increased thermogenesis.

After what has been said the reader will hardly be surprised to hear that sometimes the temperature rises in cases of *functional disease of the central nervous system.* Occasionally severe epileptic fits may be followed by pyrexia. A temperature of 109° has been recorded, and pyrexia may be observed in the status epilepticus. Delirium tremens too may have pyrexia as a symptom; it has been observed in severe chorea and it may undoubtedly be a symptom of hysteria, but the diagnosis of hysterical pyrexia should only be made after several thorough examinations, after observation for at least a fortnight, and after every other possible cause for the pyrexia has been excluded, for certain specific fevers, especially typhoid fever and tuberculosis, are very liable to mislead.

The central nervous system is more often damaged in cases of hyperpyrexia than in cases of pyrexia, for Dr. Bryant has shown that out of a hundred consecutive cases in which the temperature rose over 106°, eleven were due to injury to the brain, three to cerebral tumour or hæmorrhage, six to injury to the spinal cord, and one to myelitis, in all 21 per cent, and hyperpyrexia occurred in 2.18 per cent of all cases of fractured skull. The hyperpyrexia of meningitis (it occurs in 3.4 per cent of all cases of meningitis) may be partly due to direct injury to the central nervous system. It may be well here to remind the reader that hyperpyrexia is most common in the hottest months of the year. Out of Byrant's hundred cases twenty occurred in August and fifty-one in the months of June, July, August, and September. But this is not surprising, for it is then that the central nervous system has greatest work, even in health, in adjusting the production of heat to the loss.

Many writers have thought that the pyrexia which follows severe peripheral irritation, viz. that which occurs during gallstone colic, or

that of catheter fever, is due to the action on the central nervous system of the strong peripheral impulse.

(ii.) The second variety of pyrexia, that which results from the introduction of a poison into the body, acts through the circulation carrying the poison either to the parts of the body connected with the production of heat or to those connected with the loss. The most active known pyrexial-producing poison is B. tetrahydronaphthylamine; I have seen the injection of it subcutaneously into a rabbit cause a rise of 10° F. in one and three-quarter hours. But, as already mentioned, the most interesting clinically of the fever-producing agents are micro-organisms and the toxins they manufacture.

Much attention has been directed to the question whether the pyrexia in these cases is beneficial to the sufferer, and it is obvious that this question is of the highest importance. Some micro-organisms, which are very harmful to the human body, have their activity much lowered by a temperature not very greatly in excess of that of health; thus Koch found that if tubercle bacilli were kept at a temperature of 107.5° F. for three weeks their development was much hindered, whilst the best temperature for them was 99.5° F. Parallel observations have been made upon the pneumococcus and the spirillum of relapsing fever. Pasteur and Wagner observed that fowls, ordinarily refractive against anthrax bacilli, succumbed if their temperature was artificially lowered. On the other hand, other observers have shown that animals artificially warmed seemed able better to withstand certain specific fevers. Loewy and Richter state that rabbits whose temperature is raised by damage to their corpora striata are the better able to resist diphtheria, fowl cholera, swine erysipelas, and pneumonia. These observations, although not proving that the production of pyrexia is a protective mechanism, certainly suggest that it is, and the fact that antipyrin, acetanilide, phenacetin, and other antipyretic drugs have not been found in any way to benefit fevers, though possibly lowering the temperature, points in the same direction. It is true that ague is benefited by quinine, and rheumatic fever by salicylates, but these drugs are not of use because they are antipyretic, but because they are direct poisons to the cause of the disease. Typhoid fever is certainly benefited by the reduction of fever by cold, but there may be a special reason for this. Of course, it does not follow from this view (that the production of pyrexia is a protective mechanism) that the higher the temperature of the body the better the prognosis, for the higher temperature might be taken to indicate that the dose of infection was very severe, and that therefore the body did all it could to resist the invasion, nor would it follow that if the temperature did not rise much the dose of infection was slight, for it might be that the body was feeble, and had but little power of raising its temperature and therefore defending itself.

Much attention has been directed to the disorder of nutrition in

fever. Some attempts have been made to find out whether the amount of CO_2 exhaled during specific fevers is increased. Many more observations will have to be made on different fevers before the results can be accepted as final, but so far as they go they show that in man the amount of CO_2 excreted during fever is not increased. Thus Loewy, experimenting on a patient suffering from typhoid fever, found that when the temperature was raised the output of CO_2 in cubic centimetres per minute was on different occasions 183, 221, 190, 205, 198, 248. Three weeks later, when the temperature was normal, the output was 277. The balance of evidence, too, is that in fever the respiratory quotient is unaltered.

Here, in passing, I should like to call attention to the fact that Mr. Hopkins and I found that there was also no increased excretion of CO_2 when the temperature was raised by lesions of the corpus striatum; on the other hand, Dr. Pembrey and I found that when the temperature rose coincident with the awakening of a hybernating dormouse, there was an enormous increase in the output of CO_2. This goes to confirm the view that the metabolic processes of fever are not merely an exaggeration of normal processes, but of a different nature, and if this view should prove to be true it is of primary importance in the consideration of fever.

The discharge of nitrogen by the kidneys in fever has long been known to be greater than it would be in health on the same diet. This, of course, points to an increased destruction of proteid tissues; in itself it does not necessarily show that the increased proteid katabolism leads to a total greater production of heat, for there may be a lessened katabolism of fats. May has, however, recently worked out the subject most thoroughly in the case of rabbits affected with swine erysipelas. It will be remembered that the complete burning of a gramme of albumen liberates 5550 gramme calories (centigrade), but in our bodies albumen is only broken down as far as urea, and a gramme of albumen broken down thus far yields about 4000 gramme calories. The energy-yielding power of a gramme of fat is about 9500, and that of a gramme of carbohydrates about 4000 gramme calories. If we know the amount of nitrogen and carbon excreted by an animal, we can calculate back what must have been the amounts of proteid and fat to produce these quantities of carbon and nitrogen, and then we see how much energy this breaking down must have yielded. We can compare results if the animals are kept quiet in a cage, and the energy of the cardiac and respiratory muscular contractions need not be considered, for that chiefly becomes heat as it has to overcome friction. Working on these lines, May has shown that when a starving rabbit's temperature is raised by swine erysipelas, there is an increased katabolism which falls exclusively on the proteid tissues, and represents an increase of about 30 per cent in the liberation of gramme calories. The fat

metabolism is unaltered, therefore we learn that there is in these animals an increased production of heat in swine erysipelas due to an excessive destruction of proteid.

Appearances after death.—The cells of the tissues, especially the muscles and glands, are after death often cloudy, somewhat swollen, and appear to have undergone parenchymatous degeneration. The heart may be dilated, and this has been ascribed to degeneration of the cardiac muscle. The spleen is frequently enlarged and soft, the blood may be imperfectly coagulated, and sometimes post-mortem staining of the heart and large arteries is very evident. But any or all of these changes may be absent, and we know nothing of their cause; sometimes it would appear that they are due to the direct action of the microbic poisons on the tissues.

Treatment of fever.—Unless the pyrexia is very trifling, the patient must remain in bed. He should have milk and light farinaceous foods, partly because his powers of digestion are very impaired, and partly because May has shown that the administration of carbohydrates most markedly saves the destruction of proteid tissues. The quantity will depend upon his power of taking food, but all fevered patients require as much as they can take without upsetting them, therefore meals should be very frequent but small, and it should never be forgotten that Dr. Todd has made himself immortal because he "fed fevers." Constipation often requires relieving by some mild aperient, and sleeplessness may necessitate giving a hypnotic, and as a general rule opium is the best. Barley water and lemonade or imperial drink (acid tartrate of potassium 60 grs., gluside 1 gr., oil of lemon 3 m., water 1 pint) often relieve the distressing thirst of fever.

The sickroom should be light, airy and quiet. Its temperature should be about 55° to 60° F., and whenever possible the windows should be open.

If any drugs are required they will be mentioned in the description of each fever. Those, such as antimony and aconite, formerly given with the object of reducing the pulse, should never be ordered, and antipyretic drugs do harm.

Whatever the fever, if the temperature be so high as in itself to be dangerous to the life of the patient, the condition is called hyperpyrexia, and usually this term is applied to any temperature over 106° F. The prognosis is then very grave; 84 per cent of all patients whose temperature exceeds 106° die, and unless the patient is obviously at his last gasp cold must be applied promptly and resolutely. Occasionally in children, in whom the temperature fluctuates easily, cold sponging may suffice. For instance, a child aged five was under my care for pneumonia; the temperature was often between 104° and 105°, and on one occasion 106.4°. Under treatment by cold sponging and ice poultices the patient recovered. But in nearly all cases a cold bath

must be employed. For an adult, whose temperature is over 106°, that of the bath should be between 70° and 75°; for children it may be a little higher. The patient should be lifted into it in a sheet. The water should be stirred, and when the rectal temperature is 100° or 101° he should be taken out and put back to bed with a sheet over him. The usual duration of the immersion is ten minutes, but it is often longer. If he is collapsed after the bath, hot-water bottles and strong brandy and water are necessary. In private practice a cold bath may be improvised by putting a large mackintosh sheet under the patient, banking it up with pillows so that he lies in a trough, raising the head end of the bedstead, and pouring cold water in at the head of the trough, and letting it run out at the foot into a pail. For hyperpyrexia the cold bath, unless the shock of it is too severe, is much more efficacious than the tepid bath (90-95° F.) gradually cooled.

W. Hale White.

BOIL AND CARBUNCLE

Pathology.—Formerly boil (furuncle) and carbuncle were described separately, but it is no longer necessary, since they are similar affections, arising from the same causes, and differing merely in degree. All intermediate stages may be seen, from the simple boil to the diffuse and destructive carbuncle. The exciting cause in all cases is the *staphylococcus pyogenes aureus*. If the inflammatory and necrotic changes remain localised to a hair papilla and its sebaceous glands a boil results, but if they extend widely to the neighbouring cellular tissue and cause it to die *en masse* a carbuncle follows. In 1880 Pasteur showed the existence of a microbe in boils which he believed to be identical with that found in osteomyelitis, and his observations were confirmed by Ogston and others. It is an interesting clinical fact that patients the subjects of acute osteomyelitis have often had at some previous period a crop of boils. Such also may be experimentally produced by rubbing the skin, on the back of the forearm for example, with osteomyelitic pus. In some cases, if the local infections become confluent, a carbuncle results. Some stress has been laid on the fact that if in acute osteomyelitis the infection be of a mixed nature, *i.e.* if streptococci as well as staphylococci are found, the disease is more intense, and it is possible, but not yet clearly proven, that such is the case in carbuncle of the diffuse variety, which often runs a fatal course.

It is, therefore, evident that the clinical distinctions made between boils and carbuncles as to shape, size, and the number of openings, have lost their significance, except the fact that the area of inflammation indicates the extent of subcutaneous tissue involved, and therefore the gravity of the affection.

There are certain **etiological** points of interest and importance in addition to the *rôle* played by the staphylococcus pyogenes aureus. Both boil and carbuncle are more common in the male sex, and affect regions where the pilo-sebaceous follicles are most numerous and have large orifices. Such regions are the back of the neck, the back, the gluteal region, the perinæum, the axillæ, and the dorsal aspect of the first phalanges of the fingers. Boils are often seen on the face in the male sex, and if on the upper lip and of large size may develop into facial carbuncle. It is a curious fact,

however, that carbuncle is occasionally seen on the palms of the hands and soles of the feet, which are quite hairless, but have large, widely open, sudoriferous glands. In some occupations boils are common: thus cavalry soldiers and rowing men are prone to furunculosis on the gluteal region; infantry men to boils on the neck from the rubbing of the stiff "stock"; tanners and post-mortem attendants on the backs of the hands. In the case of the first two the staphylococci are present in the clothes, and are rubbed into the pilo-sebaceous follicles by constant friction. Individual liability is well marked. One man will suffer if he eat too much meat, another if he eat too little, while a third may indulge in all vagaries of diet and not have a single boil. In others, a dyspeptic attack or prolonged constipation is surely followed by furuncles. After typhoid fever, furunculosis and carbuncle are not uncommon.

The chief interest, from a medical point of view, lies in the association of boil, carbuncle, and glycosuria. It has been shown that if to a dose of staphylococcus culture, too feeble by itself to provoke suppuration, a certain quantity of grape sugar be added, the culture rapidly acquires marked pus-producing properties, and it is a noteworthy fact that boils are very common amongst those engaged in sugar refining. So firmly has the connection between carbuncle and glycosuria, whether diabetic or not, been insisted upon, that it is often the presence of the former which calls for an examination of the urine. It must, however, be remarked that sometimes no sugar is discovered, or, if it be, its presence is merely temporary, and it disappears when the carbuncle has healed. In many instances it is impossible to doubt the connection between the two, but reliable statistics are required to show the exact frequency of the incidence of carbuncle in diabetes, and how often sugar is temporarily present in cases of carbuncle. Some other abnormal states of the urine are also found when carbuncle is present, notably albumen, excess of phosphates, excess of uric acid, and diabetes insipidus. Alcoholics often suffer from boil and carbuncle; and finally a hemiplegic limb is not seldom the site of an eruption of boils.

Symptoms.—These affections are characterised by the following symptoms:—A boil commences as a small itching red papule, with a depression at its summit, from which a hair is seen issuing. In about four days the swelling has much increased, and is conical, and the seat of considerable boring pain. Up to this time the swelling is indurated. In some cases no softening occurs, and the

boil is then said to be blind; but more frequently pus begins to form from the fourth to the sixth day, and on the ninth or tenth day the slough, consisting of the necrosed hair follicle and sebaceous gland, and some surrounding tissue, is discharged. The constitutional symptoms are not, as a rule, marked. The onset of a carbuncle is often preceded by some malaise, and the general symptoms are well defined. In some instances there are rigors and fever, and the symptoms are of a pyæmic character; in others there is a condition of collapse, subnormal temperature, and feeble pulse. Locally, the site of the impending carbuncle feels hot and is painful, and soon becomes red; then swelling of the skin occurs, at first limited, but slowly increasing. This swelling is hard and red, and gradually becomes dome-shaped. In four to six days several vesicles containing blood-stained pus and serum appear; these vesicles break, and soon openings leading to the subcutaneous slough are formed. Meanwhile, the area of redness, œdema, and pain has increased, and the parts present the appearance of acute inflammatory tension. The openings may coalesce, and a large crater, with the slough at the bottom, is formed; or, if it is thought expedient, the skin between the orifices may be divided, and a free aperture made for the exit of the slough.

Complications and prognosis.—A boil situated over a large venous trunk becomes dangerous on account of the possibility of phlebitis; and the so-called malignant facial carbuncle, beginning as a boil on the upper lip, may result in septic phlebitis of the labial, angular and orbital veins, and of the superior longitudinal sinus. If the head, chest, and abdomen are affected, especially in diabetic subjects, meningitis, pleurisy and empyema, and peritonitis may ensue. One case is recorded where a carbuncle sloughed through the whole thickness of the abdominal wall, exposing the viscera. The prognosis of these affections, therefore, depends upon the region affected, the extent of surface involved, and the general condition of the patient, especially as to glycosuria, albuminuria, gout, and alcoholism. It is in diabetic subjects that the diffuse, very virulent carbuncle is occasionally seen. Diagnosis must be made between boil or carbuncle and anthrax. In the latter no pus is found, and the appearance is characteristic—a central black slough, a ring of vesicles, and a hard inflamed base.

Treatment must be general and local. Careful, well-regulated, and easily assimilated diet, avoidance of constipation, fresh air and exercise, and frequent skin bathing, are called for. Intestinal antiseptics, such as β-naphthol, salicylate of bismuth, are of value, and

later iron and quinine. Yeast has been vaunted as a specific, and nuclein internally may be of value. Alcohol, in the form of Burgundy, or port wine, or stout, is useful in feeble subjects; but it should be prohibited in those given to excess. For the diabetic, opium and codein are indicated. Locally, the treatment of boils must be on antiseptic lines, and poultices are to be avoided; the surest means to ensure crops of boils is to use poultices. The skin in the neighbourhood of a boil must be protected by collodion, and the boil should be fomented with hot boracic lotion, and, when ripe, incised. Hot lead and opium lotion will often relieve pain.

The local treatment of carbuncle presents many difficulties. On the one hand we have to guard against, especially in diabetics, the effects of prolonged pain and the possibilities of septic absorption, owing to the retention of the slough; and, on the other hand, an incision is often fraught with danger owing to the hæmorrhage. Some have thought injection of carbolic acid and glycerine to be of service; but, with damaged kidneys, it is not advisable to do this. It seems that in localised carbuncles frequent hot antiseptic applications will facilitate the separation of the slough, and if much pus be present, a limited incision is advisable. In large diffuse carbuncle a small, not crucial, incision in the centre may be called for; and, to avoid the risk of hæmorrhage, the various apertures may be joined by the thermo-cautery. Every effort must be made to sustain the patient's strength, but many patients with diffuse carbuncles resist all treatment.

A. H. Tubby.

ERYSIPELAS

Erysipelas is an infective inflammation of the skin caused by the invasion of the lymphatics by the *streptococcus erysipelatos*, accompanied by pyrexia and other constitutional disturbances. The inflammation may spread from the skin to the adjacent mucous membranes, or it may start in the latter and extend thence to the skin.

Pathology.—The relationship between erysipelas and various forms of cellulitis, septicæmia, and pyæmia is still a debatable question. Some hold that erysipelas is a distinct disease, while others consider it to be a variety, due to special localisation, of a

disease which has other manifestations. The latter view is adopted here for the following reasons, viz. first, that erysipelas does not always "breed true," for instance, a case of erysipelas may give rise in other patients to cellulitis, puerperal fever, or some other form of septicæmia; secondly, that a case of typical erysipelas may gradually develop into one of cellulitis, or even of pyæmia; and, finally, that the streptococcus erysipelatos, which is the cause of erysipelas, is identical with the streptococcus pyogenes, which is the cause of many forms of septic disease.

A section through the affected skin shows that the lymphatic vessels and spaces at the spreading margin of the inflamed area are filled with micrococci arranged either in pairs (diplococci), or in chains (streptococci). In the rest of the affected area there will be found a serous and cellular infiltration, by means of which the micrococci are ultimately destroyed. The inflammation spreads along, and as a rule remains limited to the skin, because the micrococci can travel more readily along the lymph spaces than in any other direction. Should they reach the subcutaneous tissue, a cellulitis is produced; and should they get into the circulation, a septicæmia or pyæmia will arise.

Bacteriology.—From the affected skin it is easy to cultivate the *streptococcus erysipelatos* causing the disease, which possesses the following characters:—It consists of cocci arranged in pairs and in chains, the latter being frequently very long and convoluted. It stains with the ordinary dyes, and is not decolorised by Gram's method. It grows readily in all the ordinary media, both in the presence and in the absence of oxygen, either at the usual temperature of the air, or at the temperature of the body. On the surface of solid media, the colonies are characterised by being small and discrete; and they do not liquefy gelatine. In broth the growth sometimes occurs as a uniform turbidity, more frequently as a flocculent mass which falls to the bottom of the tube, leaving the supernatant liquid clear.

Fehleisen, by successfully inoculating individuals with pure cultivations, in the hope of curing them of malignant tumours, furnished the direct proof that the streptococcus is the cause of erysipelas.

So far as animals are concerned, the virulence of the streptococcus, and consequently the effect produced by inoculation, varies. In rabbits inoculation of the skin of the ear may produce a condition similar to that of erysipelas in the human subject, while septicæmia or suppuration may be produced by subcutaneous inoculation with cultivations of appropriate virulence. Frequently a streptococcus

isolated from a severe case in the human subject is found to be almost harmless to laboratory animals. The streptococci obtained from various cases of erysipelas differ from one another not only in virulence, but also to some extent in cultural characteristics. It would, however, appear that these different varieties can be reduced to a uniform type by special means.

By some the *streptococcus pyogenes*, which gives rise to septicæmia, puerperal fever, etc., and the *streptococcus erysipelatos* are considered to be distinct micro-organisms. This view is based partly upon the different effects produced in animals by inoculation, and partly upon differences in cultivations. The more we know about the various types of both micro-organisms, the less important do these differences become; and the most generally accepted view at the present time is, that the streptococcus erysipelatos and the streptococcus pyogenes are identical. Consequently, erysipelas cannot be looked upon as a distinct specific disease, although it may be described as a clinical entity on account of the special symptoms produced by the localisation of the micro-organisms in the skin.

Etiology.—Erysipelas occurs in almost all parts of the world; it attacks persons of all ages and of either sex, and it appears to be more prevalent during the colder seasons of the year. Patients suffering from chronic Bright's disease, or from the effects of chronic alcoholism, and those living under bad hygienic conditions are especially liable to be attacked. Some individuals are exceedingly susceptible, and are attacked again and again. It is difficult to decide whether such cases are due to fresh infection, or whether they are recrudescences of the disease. Whatever may be the explanation, the protection afforded by one attack is but slight, and of short duration.

The most common mode of infection is by means of a wound in the skin; and, before the days of antiseptic surgery, erysipelas, when introduced into a surgical ward, rapidly spread, the virus being no doubt conveyed to the wounds by the fingers of those in attendance. At the present time erysipelas is almost unknown after surgical operations. It occasionally follows on vaccination.

Patients are sometimes attacked when there is no obvious wound for the entrance of the virus. Probably in such there was some abrasion of the skin, which had disappeared at the time of observation. In some cases the virus enters through the mucous membrane of the fauces or other parts, and spreads by direct continuity to the skin.

After infection there is an **incubation period** of from one to three or four days, during which no symptoms are observed.

Apart from wounds, the face is most frequently affected, although any part of the body may be attacked. In the face the disease usually arises at the junction of the skin and the mucous membrane, near the side of the nose, the inner canthus of the eye, or the margins of the lips. The affected skin becomes red, swollen, painful, and tender. The inflammation spreads by direct continuity to the adjacent skin, the edge dividing the affected from the healthy skin being raised and well defined. In parts where the skin is closely adherent to the subjacent tissues, the spread of the inflammation is arrested. As the inflammation advances the redness disappears from the part first affected. Where the skin is loose, as on the eyelids and the scrotum, the swelling is intense. Vesicles and bullæ frequently appear over the affected area. The inflammation lasts for about a week, and, as it subsides, the skin becomes flaccid and shrivelled, the vesicles dry up, and desquamation occurs. When the scalp is affected there is considerable œdema, but not much redness. The lymphatic glands in the neighbourhood of the affected skin are usually tender and slightly enlarged.

When a mucous membrane, such as that of the fauces, is attacked, it becomes swollen, and brawny, and of a deep red colour.

Symptoms.—The onset of the disease is usually quite sudden, with rigors and vomiting. The temperature quickly rises to about 104° F., and there are the usual accompaniments of fever, headache, loss of appetite, etc. Albuminuria is generally present, and nephritis is by no means uncommon—blood and casts appearing in the urine. Diarrhœa is often a troublesome symptom. Herpes labialis and sore throat are of occasional occurrence.

In favourable cases the temperature falls in about six or eight days, either by lysis or more frequently by crisis; the inflammation of the skin ceases to spread, and the other symptoms quickly subside. In unfavourable cases the pyrexia may be high, or the patient may fall into a typhoid condition, becoming wildly delirious, and succumb with severe nervous prostration, or he may die from exhaustion with vomiting and diarrhœa.

In addition to the acute form of the disease, a more chronic form occurs. In this type the inflammation of the skin may wander about from one part of the body to another; the constitutional symptoms are not as a rule severe, and there is often little or no pyrexia.

Relapses occurring shortly after the first attack are not at all uncommon. With the relapse the temperature rises, and fresh inflammation of the skin sets in.

Certain **complications** may arise during an attack of erysipelas. The inflammation may spread to the larynx, causing serious obstruction to the respiration; or it may spread to the lungs, producing bronchitis and pneumonia. By the escape of the streptococci into adjacent parts, various septic conditions may arise. The most frequent of these is diffuse cellulitis; but other septic conditions, such as meningitis, peritonitis, pericarditis, pneumonia, or even pyæmia, are by no means unknown.

An attack of erysipelas may give rise to a blocking of the lymphatics, and thus cause permanent œdema. This is especially frequent in the subcutaneous tissues below the eyes, where large bladder-like swellings may occur. Erysipelas of the scalp often causes loss of hair. Sloughing of the cornea and suppurative otitis have been met with as later results.

A beneficial influence is sometimes exerted by an attack of erysipelas upon chronic skin diseases and certain varieties of sarcoma; in fact a complete disappearance of the latter may occur, so that inoculation of patients with erysipelas has been performed with a therapeutic object. It was found, however, that the erysipelas thus set up was too severe to justify a continuation of the treatment. The toxines produced by the streptococcus erysipelatos are now employed with the same object. The toxines are prepared by cultivating the streptococcus and the bacillus prodigiosus together in broth. The bacteria are separated by filtration through porcelain, and the filtrate used for injection (Coley's fluid). The effect of the injections is to cause pyrexia and general malaise, and in a number of instances the tumours have disappeared.

Diagnosis.—Erysipelas is usually quite easy to diagnose, the red swollen skin, with a well-defined raised edge, accompanied by pyrexia and constitutional symptoms, being quite unmistakable. The difficult cases are those in which the disease assumes a chronic type, with slight or no pyrexia. Commencing herpes on the face may resemble erysipelas, but the rapid appearance of vesicles and their distribution quickly clears up the diagnosis. Various forms of erythema can be distinguished by the absence of severe constitutional disturbances, and by some distinctive peculiarity in the character and distribution of the patches. An erythema occurring during the course of Bright's disease may give rise to difficulties in diagnosis. Acute eczema is easily distinguishable by the nature of the lesions.

In cases of doubt, a cultivation taken from the affected area of skin will settle the diagnosis.

It is not proposed to discuss the differential diagnosis between erysipelas and diffuse cellulitis, as the diseases are considered to be etiologically identical.

Prognosis.—In the aged, and in patients suffering from Bright's disease, chronic alcoholism, or some other debilitating disorder, the prognosis is unfavourable. It is less favourable in patients suffering from wounds than in those in whom the disease appears to be "idiopathic." Erysipelas starting at the umbilical cord in infants is of bad prognosis. Unfavourable symptoms are severe pyrexia, delirium, the typhoid state, severe vomiting, and diarrhœa.

Treatment.—The treatment of erysipelas falls under three headings—general, local, and specific. The general treatment is such as is applicable to all fevers. The patient should be put upon a light nutritious diet, and stimulants should be administered as may be necessary. Drugs do not cut the disease short, but iron is stated to be beneficial. The best local treatment is to apply a powder, consisting of zinc, starch, and boracic acid, over the inflamed skin, and to exclude the air by lint and a bandage, or, in the case of facial erysipelas, by a mask. Lead and opium lotion is useful for relieving pain. Painting a band with solid nitrate of silver at the edge of the affected area sometimes prevents the spread of the inflammation. Should diffuse cellulitis arise, incisions may be required.

The specific treatment consists in the injection of antistreptococcic serum. This serum is that of the horse, immunised to the streptococcus by repeated inoculations. It should be injected into the subcutaneous tissue once or twice a day, in doses of 20 c.c., strict antiseptic precautions being taken. In some forms of streptococcal infection the serum is certainly beneficial, but at present the results with erysipelas are somewhat doubtful. It may reasonably be expected that a more efficacious serum will be ultimately obtained.

J. W. Washbourn.

SAPRÆMIA, SEPTICÆMIA, PYÆMIA

Until a comparatively recent period any description of pyæmia and the allied diseases would have been almost out of place in a text-book of medicine, but in the present day, when antiseptic methods have practically revolutionised surgery, it has come to be recognised that many of the septic conditions—the so-called blood poisonings—have to be reckoned with chiefly as the result of absorption from internal cavities rather than as arising from absorption from external wounds produced by accident or by the surgeon; and although in certain cases it may be necessary for the surgeon to interfere, most of the cases of so-called blood poisoning, now recognised, come under the observation of the physician or the obstetric physician rather than into the province of the pure surgeon.

During the early transition period of bacteriology, and as the result of the work of Panum with his "sepsines," and Selmi with his "ptomaines," there crept into medical momenclature two terms to indicate what originally was spoken of as "blood poisoning"—pyæmia and septicæmia, the former including acute pyæmia, in which metastatic, usually miliary, abscesses are formed in different organs and parts of the body, and a chronic form in which abscesses appear fewer in number, of larger size and slower growth, and often localised around the joints. Under septicæmia were included all other cases of septic poisoning not followed by the formation of purulent foci. This was a most useful classification from the clinical point of view, and especially when our knowledge of the action of microbes and their products was both more restricted and less accurate than it now is. With our present knowledge of the relations of micro-organisms and their products to disease processes it is necessary to divide into three groups the constitutional and general symptoms produced by the entrance of the products of these microbes, alone or along with the organisms that produce them, into the living body. First are those states determined by the absorption of the poisonous products of bacteria from a localised manufactory, the organisms remaining localised but the poisons being absorbed and carried to various parts of the body. This condition, known as SAPRÆMIA, or true toxæmia, depends entirely on *the invasion of the system by the poisonous products of bacteria.* The organisms themselves remain in the

wound, or it may be in the hollow organ in the altered secretions of which they are flourishing, but they produce active toxic agents which are rapidly absorbed into the fluids and tissues. Kill the organisms in the wound, or wash out the cavities in which they are flourishing, and the sapræmic or toxic symptoms are immediately relieved or entirely removed. The poison does not multiply in the blood; it simply acts as an absorbed chemical substance, and unless the initial dose be large or of exceedingly lethal character the patient may recover as soon as the local manufactory is closed or done away with. Examples of this sapræmic condition are diphtheria and tetanus, although multiplication of the poison-producing organisms may sometimes take place in the tissues. The real sapræmic condition is that in which there is absorption of the formed poison from without, as in very acute cases of tetanus, where the poison is produced entirely outside the body, or in cases of absorption from the intestines of the poisonous substances produced by rapidly multiplying organisms, which may be likened to the vegetable alkaloids as regards the toxic effects they set up. Exactly the same process may be observed in the post-partum toxæmias or sapræmias, resulting from the putrefactive changes that occur in remnants of the placenta, or in clots left in the uterus; or again as the result of absorption from a localised abscess, or any mass of dead and decomposing tissue within the body. When operations were performed without antiseptic precautions, toxic absorption was one of the causes of the fever and collapse that so frequently and shortly supervened.

The organisms which produce many of these poisons are entirely saprophytic and can never invade the body themselves; their products, gaseous or liquid, however, appear, as already mentioned, to have the power of poisoning tissue cells and thus of preparing the way for the advance of the true pathogenetic organisms into the tissues. Panum, Selmi, Burdon Saunderson and Koch ascribe certain very definite symptoms and conditions to what are called sepsines or ptomaines (alkaloids which are produced by the action of putrifying organisms on animal tissues or fluids). Putrid solutions containing these substances still remain poisonous after they have been boiled, showing that the action is not due to the presence of micro-organisms, or even of enzymes, but to other more stable chemical substances produced by them. It is probable that in addition to those that are unaltered by heat, there are others similar to the diphtheria and tetanus toxins, which contain, in addition to ptomaines, enzymes or ferments, some of

which have a very poisonous action, although it takes some time for this action to become fully developed. It is interesting to notice that these ptomaines injected into animals give rise to fever, gastric and intestinal disturbance, muscular irregularity, weakness, and increased, or sometimes diminished rate in respiration and pulse, not always but frequently similar to those met with in the human subject in cases of sapræmia, the differences being apparently due to the difference in dose. Collapse in the ordinary sense of the term may be said to be the most marked feature following the injection. Certain of these poisons apparently exert a direct action on the endothelium of the blood vessels and even upon the corpuscles, these cells undergoing marked degenerative changes.

Symptoms.—As in cases of diphtheria, the poison formed by the organisms at the seat of the wound exerts a depressing influence not only on the tissue near the wound, but also in distant parts of the body, with the result that these tissues are rendered much less capable of resisting the invasion of other organisms that have found their way to the wound. Similarly absorption of toxic substances by the walls of the larger cavities may produce marked depression and materially diminish the general powers of resistance, sometimes even causing collapse or recurrent shock, where the absorption goes on very rapidly, but intermittently. It has been noted by the surgeon that where absorption has taken place from a wound that has not been kept clean, the first symptoms make their appearance soon after any change is observed in the wound itself; the temperature rises three or four degrees; rigors often occur (though these may be absent); afterwards headache, vomiting and great thirst supervene; the skin, at first pallid, becomes flushed, hot and dry, and the pulse and respirations increase in rapidity. Beyond these and some symptoms of intestinal irritation, nothing may be observed, and the patient may quickly recover. In more marked cases the patient becomes rapidly worse. Watson Cheyne, in describing this condition, says: "There is excessive muscular weakness, as evidenced by tremors; the tongue is now dry, brown and very tremulous; the mouth and lips are covered with sordes; diarrhœa may come on and motions and urine be passed unconsciously. The skin may be slightly jaundiced and petechiæ may appear. The temperature may fall even to subnormal; coma comes on and gradually deepens into death. Death usually occurs about the second or third day of the disease, but in other cases may be postponed for another week, the patient passing into a typical 'typhoid state' and dying of exhaustion."

The **diagnosis** is comparatively easy from the fact that the symptoms are so marked and bear such a definite relation to changes in wounds, accumulation and decomposition of secretions, etc., in cavities and the like. It is maintained that the shock which makes its appearance where large surfaces are exposed to the action of septic material, especially when it occurs on the second or third day of such exposure, is due almost entirely to this sapræmic condition.

If it is possible to remove the local source of the poison, or to remove the substances in which the organisms are growing, the **prognosis** should always be favourable, except in patients of low vitality. The sapræmic condition, however, by increasing the vulnerability of the tissues, renders the patient peculiarly liable to be attacked by septicæmia.

The **treatment** in such cases is evident. Remove, as carefully as possible, by curetting, free drainage, and by constant irrigation with warm sterile water or weak antiseptic lotion, the substances in which the organisms are growing. General medical and surgical treatment should also be attended to, and the strength of the patient kept up by means of nourishing, but non-stimulating diet.

Septicæmia differs in certain essential details from sapræmia, although it must really be looked upon as an extension of that condition. The characteristic feature of septicæmia is that it is brought about by the *entrance into the vascular system of active micro-organisms along with their poisons;* consequently the condition may be very prolonged, the prognosis as a rule being much more grave. The gravity of the condition consists in the fact that the active micro-organisms are able to exist and multiply within the body where it is impossible to get at them for the purpose of diminishing their vitality, and of there continuing to carry on the manufacture of the poisonous substances which are the active agents in bringing about devitalisation of the tissues.

In a case of sapræmia, as soon as the local manufactory of the poison is removed, the patient, if the process has not gone too far, commences to recover, since there is no further production of poison. In the case of septicæmia, on the other hand, the original local manufactory may be removed, but the formation of the poison is still continued by the organisms that have found their way into the body. The onset of the disease may be much slower, as the invading organisms may take some time to make good their position in the tissues and fluids of the body, and until they are able to do this they are incapable of manufacturing any very large quantities of

poison. It is quite possible that the distinction between sapræmia and septicæmia might be broken down, were it not that in cases of septicæmia pyogenic cocci, few in number, no doubt, may usually be found in the blood; though, did not the production of the poison go on after the local manufactory had been removed, one might imagine that the presence of such organisms was merely accidental. On examining the organs of such a case of septicæmia, however, long before the abscesses have been found, there may usually be demonstrated in the kidneys, sometimes in the liver and lungs, and more frequently in the tissues of the heart, a number of micro-organisms usually staphylococci or streptococci, though here and there bacilli may be found. In one case of hæmorrhagic septicæmia that I examined, both bacilli and cocci, singly and in masses, were present in large numbers in the capillary vessels. Perhaps the most common of the septicæmias are those of purulent origin; those following certain specific infective febrile diseases, especially of the exanthematous type; those following wounds, particularly post-mortem and dissecting wounds, the septic organisms appearing to assume a special virulence in the tissues and fluids of dead bodies, and of patients that have suffered from purulent inflammation of the serous surfaces of the joints, peritoneum or pleura. In certain cases, lowered vitality of the tissues appears to be almost an essential predisposing cause; devitalisation of the tissues, whether by injury, malnutrition, or action of poisons, seems to play a very important part in the production of these septicæmias; whilst, as in the case of sapræmia, anything that interferes with the free discharge from the surface of the wound, or from the cavities of the body, is also a powerful predisposing agent.

Septicæmia as a special condition is now seldom observed; but even within the last twenty-five years deaths from septicæmia following operations and in the maternity hospitals were by no means unfrequent. Badly ventilated and dirty hospitals, infected instruments, imperfect antiseptics and the like, now comparatively rare, then played an exceedingly important part in the production of this condition.

The **diagnosis** of septicæmia is, as a rule, either very easy or very difficult: easy where there is an evident wound, sometimes a very small one, merely a pin-prick, and when the process comes on, perhaps, at first slowly, but afterwards rapidly. It may commence within twenty-four hours of inoculation, with rigors, sometimes repeated, followed by a rapid rise of temperature of from 4° to 6° F.; the pulse becomes rapid, feeble, and irregular, and the heart weak; vomiting, headache, delirium, at first acute, and latterly of the low

muttering typhoid type, almost always occur; and the lungs become congested, or the patient suffers from bronchitis—in fact the patient, as in sapræmia, frequently passes into the "typhoid condition." The skin has a peculiar pallid, yellowish tinge, especially about the angles of the nostril and mouth, and there may be small subcutaneous hæmorrhages. The breath has a peculiarly sweet, new-mown-hay smell. In milder cases the symptoms are simply less marked, the skin does not become so markedly yellow, and the small hæmorrhages so characteristic of the very acute cases are not seen. Rigors also are less characteristic of the milder than of the more acute forms. Where septicæmia is the result of a small or punctured wound the organisms sometimes seem to spread, especially along the lymphatic channels, which may then become acutely inflamed, appearing as distinct red lines on the surface of the skin. There is often acute pain; and in consequence of the changes that occur in the lymphatic vessels the tissues of the limb become œdematous, the glands become tender, and afterwards may suppurate. This is not really a septicæmia, but an acute lymphangitis. If the process is not arrested at the glands nearest to the wound, the patient usually succumbs very rapidly to an acute septicæmia or pyæmia.

The **prognosis** in acute cases of septicæmia is very unfavourable. Those in robust health have a better chance of recovery than those weakened by disease, bad hygienic conditions, or impaired nutrition.

Treatment is directed to the amelioration of the symptoms; the removal of the local cause by excision, thorough drainage and irrigation, and, if necessary, cauterisation. The strength of the patient should, as far as possible, be maintained by the exhibition of suitable food, by controlling the temperature, and by relieving the pain.

In all cases of either septicæmia or pyæmia where streptococci can be demonstrated in the blood or in the tissues, or even when their presence is suspected, full doses of antistreptococcic serum should be injected as early as possible, and should be repeated as often as may be found necessary.

Pyæmia.—It has been stated that in septicæmia micro-organisms may be found in the blood; but no metastatic abscesses were described, the patient usually succumbing to the action of the acute specific poison before there has been time for the formation of abscesses.

In pyæmia, as early indicated by Lister, and later by Ribbert, it is probable that septic inflammation of a vein or veins is usually set up in the immediate neighbourhood of a septic wound. As the result

of the changes that take place in the endothelium of the vein so affected, there is usually a local deposition of fibrin in which streptococci or staphylococci may develop, sometimes in large numbers. A septic thrombus is thus formed which naturally undergoes softening, the clot going through what may almost be spoken of as suppurative changes; and as this continues, and the clot softens and breaks down, fragments set free are carried as emboli to the capillaries, where, becoming impacted, they form foci around which abscesses—sometimes very small, at other times running together into larger suppurating masses—are formed.

It was pointed out by Koch that micro-organisms finding their way into the blood may multiply or be massed together, entangling blood corpuscles, into small floating agglomerations which, carried into the capillary system, become impacted, and so form the centres of abscesses.

Here it should be borne in mind that the healthy tissues of the body have a great power of destroying micro-organisms, and to this must be attributed the fact that although septic organisms must be distributed throughout the body, and to all the organs, abscesses may be met with only in a single organ, or in the synovial membrane of a single joint. It is supposed, indeed, that by some means or other the organ affected has been deprived of its resisting power, or the tissues of the joint have had their vitality lowered by an old inflammatory condition, a bruise, or a wound. In certain cases of acute pyæmia following surgical operations, the kidneys only may be affected. For this two reasons have been assigned: the first is that in this organ there is a double set of capillaries, and that consequently the small masses of organisms which might pass through a single set of capillaries are entangled by a second set, because of the extreme slowness of the circulation at this point. A second explanation is one which receives some countenance from the experiments carried out by Sherrington and others, that the micro-organisms making their way from the capillary system into the tubules are allowed to rest, especially at points where the tissues have their vitality in any way impaired; here they increase in number, and become the centres of abscess formation.

That pyæmic abscesses are in many cases, though not invariably, the result of emboli, must now be generally accepted. They may follow on alterations in the endocardium, and the settling of micro-organisms upon the altered tissues, with a subsequent increase in size and softening of the vegetation. The secondary abscesses, the result of the impaction of emboli, are usually first manifest in the

lungs, especially when the pyæmic process commences in connection with the bones or periosteum, where apparently the emboli are larger, and are, therefore, caught more certainly in the comparatively wide pulmonary capillaries. Multiple abscesses in such cases are formed; but it is only when they are of some size, and are near the surface, that any definite signs and symptoms are obtained, being mainly those of pleuro-pneumonia and empyema.

Once a mass of pyogenetic organisms, detached from such a thrombus in a vessel or vegetation, becomes impacted, it may be the centre of a pyæmic abscess from the fact that these organisms form substances which exert a marked devitalising effect on the wandering cells which attempt to get into the neighbourhood of the organisms, and on the fixed cells that are there already. The wall of the vessel in which the micro-organisms are fixed is similarly devitalised, and the pyogenetic cocci gradually make their way through the dead tissue or vessel wall into the surrounding area, their advance being limited only by the presence of an enormous number of leucocytes which are found wandering towards them. The leucocytes near the organisms are involved in the general death of the tissues; but others come up to take their place, and gradually, if these and the tissues are moderately healthy, they form a zone of active resistant cells. In addition to the poison that causes the death of the leucocytes, the pyæmic organisms secrete a substance which has the power of peptonising or digesting the dead tissues and cells, both those originally constituting the part and the leucocytes that have come to reinforce them.

Pyæmia is now comparatively rarely met with, except as following diffuse suppurating cellulitis, ulcerative conditions of the internal organs, or suppurations near large veins, in bones, and in cavities which may become closed, or that have bony walls, such as the middle ear, the antrum or frontal sinuses, or in thrombosis of the cerebral sinuses.

Symptoms.—From the nature of the process, pyæmia must be expected at a somewhat later period than either sapræmia or septicæmia, but it usually occurs, as pointed out by Watson Cheyne, "within the first week of injury or operation."

The first symptom, of course, in surgical work, is the unhealthy appearance of the wound. The veins leading from the wound may become indurated and painful, and the area of connective tissue drained by the wound inflamed and œdematous. Before this, the patient is uneasy and feverish, loses his appetite, and usually suffers from great thirst. The bowels may be constipated, or there may

be persistent diarrhœa. After a slight rise in temperature, rigors occur, during which the temperature may rise 5° or 6° F., or even more. The rigors are followed by very profuse sweating, during which the temperature may fall to 100° or 101°, or may become subnormal. Vomiting is a fairly common symptom. There is furring of the tongue, which later becomes brown, dry, and hard—the so-called "parrot's tongue"; the teeth and the lips are covered with sordes. The action of the heart becomes weakened, the pulse very rapid, soft, feeble, and irregular. The respirations are increased in number. The muscles become soft and flabby. The patient becomes intermittently delirious, and ultimately falls into the "typhoid state." There may, however, be a more acute delirious condition, the patient usually complaining greatly of headache. Rashes resembling the scarlet-fever rash are described as occurring, first in the large folds of skin spreading up and down the limbs. Sometimes there is a "pustular rash," and "in the later stages of the disease petechiæ are not uncommon, or extensive cutaneous hæmorrhages may occur." The yellowness of the skin and the sweet-hay smell of the breath, described in septicæmia, are also present in this condition. The patients usually succumb to the disease at about the eighth to the twelfth day, though they may live longer. They die of exhaustion, and are usually comatose before death, though some such condition as meningitis, cerebral abscess, congestion of the lungs, ulcerative endocarditis, may be the immediate cause of the fatal issue.

The spleen usually becomes enlarged and tender. Abscesses may be formed, which, bursting into the peritoneal cavity, set up peritonitis. There may be multiple abscesses in the kidneys, or in the brain, often accompanied by purulent meningitis. Sudden blindness, due to plugging of the central artery, or optic neuritis with retinal hæmorrhages, may also occur. Suppuration of the serous membranes of the joints and peritoneal and pericardial cavities is frequently met with. Suppurations of the cellular tissue are fairly common.

The **Diagnosis** of pyæmia, apart from the condition of a surgical wound, an injury, or middle-ear suppuration, is often very difficult, and unless some local mischief can be traced, pyæmia may readily be mistaken for typhoid fever. Apart from the source of infection, the temperature charts are, however, usually quite different and characteristic—in the case of pyæmia the curve being irregular, whilst in the case of typhoid there is the typical evening rise and the gradual upward, but remittent, tendency of the curve during at least the first week. In typhoid fever the rigors and sweating

do not recur, and as a rule no suppurative changes supervene. The rose rash of the latter is perfectly distinct from the petechial hæmorrhages so characteristic of pyæmia.

The **prognosis** is invariably grave, especially where the disease takes the form of ulcerative endocarditis or of pyæmia of the portal system, where the secondary deposits occur in the liver.

Where no vital organs are affected, the patient may recover; but there is often considerable loss of tissue or adhesion of joint surfaces, so that deformed and stiff joints may remain.

The **treatment** of such a fatal disease is naturally of little effect; but when such cases do get well, it is because the strength of the patient is kept up, and because there is a free excision of the suppurating surfaces, a destruction of the micro-organisms in discharges by a free use of antiseptics, and in extreme cases by the removal, by dissection, of the thrombosed vein or veins, with their contained abscess-producing organisms, and thoroughly draining and washing out the resulting wounds with warm, weak antiseptic solutions.

G. Sims Woodhead.

INFECTIVE ENDOCARDITIS

The term malignant, ulcerative, or infective endocarditis, is applied to a form of septicæmia or pyæmia in which the virus especially attacks the endocardium. The inflammatory lesions in the endocardium differ essentially from those of a simple or benign endocarditis, such as is associated with acute rheumatism, in containing bacteria of various kinds. It is to the presence of these bacteria that the septic character of the symptoms is due.

Pathology and post-mortem appearances.—The bacteria most commonly present are the streptococcus pyogenes, the pneumococcus, and the staphylococcus pyogenes aureus. Much less frequently other bacteria, such as the gonococcus, the typhoid bacillus, and the tubercle bacillus are present.

These different bacteria may enter the body through the various portals by which the body is usually invaded by bacteria, through the respiratory or the digestive tract, the urethra or vagina, or through the skin. As a rule, there is some primary lesion at the seat of inoculation, and thus infective endocarditis is commonly

preceded by and occurs as a complication or sequela of such diseases as pneumonia, puerperal fever, septic wounds, etc. Less frequently there is no obvious primary lesion, and therefore no evidence of the mode by which the virus has gained entrance to the body.

A previous injury to the valves is an important factor in determining their invasion by the bacteria which have gained access to the circulation. Consequently infective endocarditis usually attacks a patient who is suffering from old or even recent valvular disease. Nevertheless, in some cases a previously healthy heart may be attacked. The valves on the left side of the heart—the aortic and mitral—are the parts most frequently affected, either one or the other, or both. Occasionally the valves on the right side are affected, though much oftener than from simple endocarditis, and very rarely there is mural endocarditis without lesion of the valves.

The inflammation of the endocardium leads to the formation of "vegetations" of a grayish colour, which may be small, or may form large fungating masses. A section through the lesion shows that it consists of a round-celled infiltration. The tissue on the surface of the valve undergoes coagulative necrosis, and a layer of fibrin is deposited upon it from the blood. In the fibrin and necrosed tissue, and to a less extent between the cells, are found the bacteria, which are the cause of the inflammation. Ulceration frequently occurs, and this may be so extensive as to cause perforation of a valve or separation of a large segment. In some cases a deep ulceration at the base of a valve may lead to aneurysmal bulging. The lesions in the endocardium differ from those of simple acute endocarditis in containing bacteria, in the tendency to necrosis and ulceration, and in the absence of reparative processes. The effects of infective endocarditis upon the patient are of two kinds, the one being due to the mechanical injury to the valves, and the other to the injurious influence of the bacteria. Valvular incompetency caused by infective endocarditis produces the same effect upon the heart and the other organs as does valvular incompetency caused by simple endocarditis, *i.e.* hypertrophy and dilatation of the heart, congested liver, œdema, and other effects of "backward pressure."

The bacteria give rise to the usual effects of septicæmia, "cloudy swelling" of the cells of the organs, hæmorrhages into the skin and other parts, acute hæmorrhagic nephritis, etc. Emboli are frequently carried from the heart to distant parts. If the embolus contains

bacteria it causes inflammatory changes where it lodges. The lungs, spleen, liver and kidneys may thus be riddled with small abscesses similar to those met with in pyæmia, and hæmorrhagic patches of inflammation may be found in the intestines. The effect of a septic embolus in a medium-sized artery may be to cause ulceration of the wall, which yields to the pressure of the blood, and thus a small aneurysm is produced. If the embolus should be free from bacteria the same effects are produced as in the case of simple endocarditis, *i.e.* infarcts in the spleen, kidneys, and lungs, cerebral softening, etc.

It will thus appear that a large number of lesions may be found at a post-mortem examination of the body of a patient dying of infective endocarditis. It is also not uncommon for a secondary lobar pneumonia to develop during the last few days of life.

With regard to the distribution of the bacteria through the body, they may be found in small numbers in all the organs and in the blood; but, as a rule, they are limited to the affected valves, and to the secondary lesions in the organs, where they are present in abundance.

The **symptoms** of the disease may be divided into two broad groups—cardiac and septic—sometimes the one and sometimes the other predominating. It will be unnecessary to detail here all the symptoms that may arise; it will be sufficient to mention the more important, a fuller description of those directly due to the heart being set forth elsewhere.

The cardiac symptoms comprise the usual manifestations due to valvular disease, dyspnœa, dropsy, albuminuria, enlargement of the liver and spleen, etc. On account of the progress of the endocarditis, the bruits are apt to change somewhat rapidly in character and fresh ones may develop. The partial detachment of a valve may give rise to a high-pitched or musical bruit.

The septic symptoms include pyrexia, which may be continuous, but is much more frequently intermittent and accompanied by rigors; profuse sweating; petechiæ and hæmorrhages into the skin, the mucous membranes, and the retinæ; the presence of blood, albumen, granular and epithelial casts in the urine; and perhaps evidence of suppuration in the lungs, abdominal viscera, the joints, or the meninges of the brain.

The occurrence of an embolism may give rise to the characteristic symptoms of infarction. If a branch of the splenic artery is blocked, the spleen becomes enlarged and tender; if the middle cerebral artery is blocked, hemiplegia occurs; and if a branch of

the pulmonary artery is occluded, pulmonary apoplexy arises, causing hæmoptysis and signs of consolidation of the lung. Should the embolus contain bacteria it will set up septic inflammation in the part in addition to its mechanical effect.

Certain clinical types of the disease may be recognised, but it would be unwise to attempt to draw a too definite line of demarcation between them. These types are the cardiac, the septic or pyæmic, and the cerebral.

In the *cardiac type* the infective process is engrafted upon an old valvular disease. A patient who has been suffering for some time with cardiac symptoms begins to manifest pyrexia, and becomes anæmic. For some days, or even weeks, the causation of the pyrexia may remain obscure, but after a time other symptoms develop which point to the nature of the case. The spleen perhaps becomes enlarged and tender; petechiæ appear in the skin; blood and casts appear in the urine; or the pyrexia assumes a septic type with rigors and profuse sweating. The cardiac symptoms undergo aggravation, and embolism may occur. The patient gradually fails, and usually dies after some months from the combined effects of the cardiac affection and of septicæmia.

The *septic* or *pyæmic* type may occur in patients suffering from old cardiac mischief, or in those with hearts previously healthy. In either case the septic symptoms are the most prominent feature of the attack, the cardiac symptoms remaining in the background. If the heart was previously healthy, bruits indicative of lesions of the infected valves generally develop sooner or later, but in some rapidly fatal cases no evidence of cardiac affection is forthcoming during life. The principal symptom is severe fever with rigors and sweating. Hæmorrhages frequently appear in the skin, the retinæ, and the mucous membranes. Blood and casts appear in the urine. The joints may suppurate and there may be cough with blood-stained sputum. The spleen is usually enlarged. There are the usual symptoms of high fever, a rapid pulse, a dry brown tongue, hurried respiration, delirium, diarrhœa, and so on. Such cases usually take a rapid course, the patient dying in a few weeks after the onset. In some cases the pyrexia is continuously high, 105° or higher, and the patient falls into a "typhoid state," so that a typhoid type has been described, but such a distinction seems to be unnecessary.

In the *cerebral type* the principal symptoms are cerebral, convulsions, headache, etc.; and in these cases meningitis is usually present.

The **prognosis** of infective endocarditis is always grave. The majority of cases end fatally. Nevertheless, recovery may ensue with permanent injury to the valves. In many cases the patient apparently recovers, but after some time—it may be months—a fatal relapse occurs.

The **diagnosis** of infective endocarditis is often difficult. Continued pyrexia arising in the subject of old cardiac disease should always be regarded with suspicion, but until more definite symptoms arise a diagnosis can hardly be made. In addition to pyrexia the most important symptoms for diagnostic purposes are petechiæ in the skin, the presence of blood and casts in the urine, and tenderness and enlargement of the spleen. Profound anæmia is also a sign of some value.

In the septic type of the disease the cardiac symptoms may be so slight that a diagnosis from septicæmia is impossible. This, however, is a matter of but little importance; for we must regard the affection of the endocardium as an accidental, rather than an essential feature of this type of the disease. The occurrence of embolism and the development of cardiac bruits render the diagnosis clear.

In any case the discovery of some source of infection, such as a previous pneumonia, or a septic wound, should aid in forming an opinion, but it must be remembered that a primary lesion is by no means always to be detected.

Perhaps typhoid fever is the disease most frequently mistaken for infective endocarditis. The tumidity of the abdomen, the presence of spots, and the temperature curve in the former, and the occurrence of emboli, a petechial eruption, and cardiac bruits in the latter, are distinguishing features. Rigors are much more frequent in infective endocarditis than in typhoid fever. In doubtful cases the blood should be tested for the "typhoid reaction," which, if present, is almost absolutely distinctive.

A bacteriological examination of the blood in infective endocarditis may enable us to say what bacteria are causing the infection. But unfortunately for diagnostic purposes the bacteria are usually absent from the circulating blood, and at the best are only present in very small numbers during life; consequently the examination frequently fails to reveal their presence. The best prospect of success is to examine a large quantity of blood—five or ten cubic centimetres. Such a quantity can readily be obtained by means of a sterile syringe from one of the superficial veins in the arm.

In the **treatment** of ulcerative endocarditis, quinine, arsenic,

and sulpho-carbolates have in some cases appeared to be beneficial, and when there is high fever the usual antipyretics may be administered. If we have evidence, either from the source of infection or from a bacteriological examination, that the endocarditis is due to the streptococcus pyogenes, antistreptococcic serum should be administered. In one case under the care of the writer, the daily administration of the serum for some weeks apparently led to the recovery of the patient. An antipneumococcic serum will probably be found useful in cases caused by the pneumococcus.

J. W. Washbourn.

GONORRHŒAL INFECTION

In addition to the urethral discharge and those more immediate complications which are treated of in surgical works, gonorrhœa is not unfrequently accompanied or followed by affections of distant parts, and occasionally of internal organs. The structures most commonly affected are the joints, tendons, and fasciæ, while less frequently observed or diagnosed as specifically gonorrhœal are such complications as iritis, conjunctivitis, sclerotitis, myositis, pleuritis, neuritis, mêningomyelitis, endocarditis, and arteritis. In some instances of these metastatic or secondary inflammations the presence of the *gonococcus* has been demonstrated and the fact of their specific origin established. The infection is, therefore, on septicæmic lines, that is to say, the specific organism finds its way to distant parts through the blood or lymph channels, and having arrived at its ultimate destination, excites secondary local mischiefs. It is possible, however, that the circulation of gonotoxin is responsible for at least some of the symptoms and phenomena of secondary gonorrhœal infection. In this connection it may be mentioned that the infection may be acquired accidentally or imparted experimentally either by inoculation with gonorrhœal discharge, *e.g.* on the conjunctiva, or by means of pure cultures of the coccus.

Of these secondary infections by far the most common or most noticed is *arthritis*, so much so that "gonorrhœal rheumatism" so-called was until quite recently the recognised term used to express the generalisation of the gonorrhœal virus. Though any and every

joint may suffer, those most frequently attacked are the knees, after which come the ankle and wrist joints, then those of the elbow, hands, and feet, and the sterno-clavicular, temporo-maxillary, and sacro-iliac.

The affection may commence at any time in the course of the urethral discharge, whether the flux be in the acute or chronic stage. Thus it may manifest itself a few days after the first appearance of the discharge, or not until this has been existing for weeks, and sometimes sets in after the complete disappearance of the urethritis.

Symptoms.—As a rule the arthritis appears suddenly, and is marked by swelling of a joint or joints, often, but not always, with redness of the skin over them, and pain and tenderness, frequently worse at night. The swelling is due to exudation not only into, but around the joint or tendon (periarthritis). The onset may be associated with constitutional symptoms, such as pyrexia, furred tongue, malaise, general pains, and other febrile phenomena. These general symptoms, however, may be absent or but little marked, more especially if the arthritis supervene when the more active stage of the discharge has passed away. The pain, though it may be severe, is usually of a dull, aching character. Inspection of an affected joint or tendon usually indicates the presence of effusion into the joint or within the sheath, and while palpation confirms this, it invariably imparts the notion of exudation into the capsule or the sheath and the adjacent parts. This condition lasts for some time, usually weeks, or even months, and the subsidence of the swelling is almost invariably accompanied by weakness and stiffness of the joint. The stiffness, partly due to exudation into the capsule of the joint and partly to adhesions, may in severe cases terminate in ankylosis and chronic osteo-arthritic changes. Though stiffness and ankylosis of joints are not uncommon sequelæ, suppuration is rare, and its occurrence may be regarded as indicating a mixed infection.

The arthritis may be multiple and is often symmetrical, as seen in affection of both knees, ankles, or hands, but this is by no means always the case, for the inflammation may be limited to one joint, tendon, or fascia of one side, and this is more common in the knee and elbow. As a general rule, when the inflammation has subsided in the affected part there is little tendency to recurrence, unless there be a simultaneous recrudescence of the discharge or the patient again contract a gonorrhœa.

Inflammations of tendons and their sheaths, of fasciæ, especially

of the back, of the thigh, and of the soles of the feet, are quite common as complications of gonorrhœa, and what has been said with regard to joints will equally well apply to them.

Though arthritis and synovitis are by far the most frequent expressions of generalised gonorrhœal infection, yet the other complications already enumerated should not be lost sight of. During the onset of gonorrhœal arthritis the patient may suffer from catarrhal ophthalmia, sometimes accompanied by iritis and sclerotitis. The injection of the sclerotic, which is quite distinct from the gonorrhœal ophthalmia due to direct infection with the urethral discharge, is regarded by some as almost pathognomonic of gonorrhœal arthritis in adults. Of recent years attention has been called to more severe and important complications, such as pleuritis, peri- and endo-carditis, and though affection of the heart is regarded as a symptom diagnostic of "rheumatism," it has been rendered certain that valvulitis may be the result of gonorrhœa, indeed one such case was followed by gangrene of one of the lower limbs, presumably embolic in nature. The writer has for years expressed the opinion that many examples of chronic arteritis, especially some cases of atheroma of the aorta, are in all probability due to gonorrhœa. Cases of myositis, neuritis, and meningo-myelitis as complications or sequelæ of gonorrhœa have been recorded. In the character of its complications it will be noted that gonorrhœa closely resembles other specific infections.

In most cases the **prognosis** is favourable, but the course of the disorder is not unfrequently lengthy and tedious. There is, however, little tendency to relapse or recrudescence. There is always the possibility of permanent stiffness, and even of ankylosis, to be reckoned with, while the occurrence of damage to vital organs should be borne in mind. Death with hyperpyrexia has been known to occur.

The **diagnosis** of the arthritis, or other secondary morbid development, must principally depend on the coexistence or recent occurrence of a gonorrhœal discharge. The evidence to be derived from a bacterioscopic examination of the urethral or vaginal discharge is of less practical value than might be hoped; for in the earlier stages there is little need for such confirmation, and in the later or chronic stages there is much difficulty in demonstrating the gonococcus. Still, it might have a negative value in cases of gouty urethritis and balanitis associated with arthritis.

The remote results of gonorrhœal infection, arthritic and other, are met with in both sexes, though probably with greater frequency

in the male. Difficulties, due to ignorance or purposed concealment, frequently arise in connection with obtaining precise knowledge in the case of females. The various manifestations predominate in young adult life, but may be met with at all previous ages. In females the coexistence of chronic uterine affection, vaginal discharge, and arthritis may suggest the real nature of the disease.

The conjunction of ophthalmia and arthritis is almost sufficient evidence in itself of gonorrhœal infection. It is in this form that the disease manifests itself in infants. Inoculation of the conjunctiva takes place at birth, a few days after which the ophthalmia appears, to be followed in two or three weeks by the arthritis. Even in such cases there is the same preference exhibited by the knees as seen in adults, and the general features of the joint affection correspond to the above description. In very young subjects the disease seems to be more amenable to treatment, and to run a course of a few weeks only, without the obstinate persistence so characteristic of its occurrence in the grown up. In older children the affections of the joints, tendons, or fasciæ may follow on accidental conjunctival inoculation or criminal vulvo-vaginal infection.

The affection of certain joints, such as the sterno-clavicular, sacro-iliac, and temporo-maxillary, which are less frequently attacked in ordinary rheumatism, should give rise to suspicion. Though gonorrhœal arthritis is not unfrequently polyarticular, it exhibits less tendency than articular rheumatism to shift from one joint (or joints) to another.

Treatment.—No specific to abbreviate the tedious and protracted course of the disease has yet been discovered. The treatment must be palliative, symptomatic, and chiefly on surgical lines; indeed the very story of the disaster clearly indicates that any urethral discharge should receive special attention. Painting a joint or tendon very freely with liq. iodi fort. sometimes has a good effect, while the withdrawal of fluid from joints which exhibit little tendency to resolution and irrigation with a solution (1 in 4000) of perchloride of mercury is to be recommended. In some cases the application of belladonna or of Scott's dressing is useful. It may be necessary to apply splints in the acute stage to keep the joints at rest, and afterwards to use friction or massage, which may be advantageously combined with the local application of dry heat. Sometimes it is necessary to break down adhesions under an anæsthetic. Should any of the more serious complications of the infection manifest themselves, *e.g.* pleurisy, pericarditis, or endocarditis, these must be treated on appropriate lines. The diet should

be nutritious and not too stimulating; the bowels must be carefully regulated. For the pain, it is best to rely on opium or morphia. The most approved internal remedies are quinine, with potassium iodide and arsenic, though occasionally guaiacum and sarsaparilla seem to do good. Ordinary anti-rheumatic remedies, such as the salicylates, have no effect.

R. G. Hebb.

TYPHOID FEVER

Syn. Enteric Fever

An infectious fever characterised by inflammation and sloughing of the solitary and agminate glands of the small intestine, enlargement of the mesenteric glands and spleen, and a roseolous rash. The disease is caused by the invasion of a specific microbe—the *bacillus typhosus*, or *Eberth's bacillus*.

Bacteriology.—The *bacillus typhosus* is a flagellated bacillus usually 2 μ to 4 μ long and 0.5 μ thick. In liquid media it shows active movements (Plate I.). It presents a very close resemblance both in structure and habit to the *bacillus coli communis*, from which, however, it is specifically distinct. It may readily be cultivated in the usual artificial media, both liquid and solid, in which it multiplies freely. It flourishes best at about the temperature of the body, 37° C. (98.6° F.). It ceases to grow below 9° C. (48.2° F.), or above 42° C. (107.6° F.). It is killed by a few minutes' exposure to the boiling point, or by half-an-hour's exposure to a temperature of 60° C. (140° F.). It will maintain its vitality for a considerable time, many days or even weeks, in water both fresh and salt, especially when sterilised, but it does not multiply in water. It will also maintain its vitality for many weeks when mixed with sand or earth and dried, and may then be blown about as dust. In soils contaminated with animal matter it will continue to grow and spread indefinitely at the ordinary temperature of the air, but in virgin soils it dies out. Exposure to sunlight impairs its vitality. It has been found alive in the pallial cavity, and in the rectum of oysters and other bivalve molluscs living in water contaminated with sewage, and it has been found to be capable of penetrating eggs immersed in liquid cultures,

It grows freely in milk and butter. When cultivated in artificial media it very rapidly loses its virulence, which can be restored and intensified to the highest pitch by passing it through the peritoneal cavity of successive animals.

When cultivated the bacillus generates poisons which are both contained in its substance and diffused in the medium. These present some differences of action, but generally when injected into the animal body they cause fever, followed by collapse, injection of the mucous membrane of the intestine, mucous diarrhœa, and fatty degeneration of the heart. The bacillus itself, when introduced either into the peritoneal cavity or subcutaneously, is capable, when virulent, of becoming diffused, and may be found in the blood, spleen, liver, and other internal organs, but shows no predilection for the intestinal glands, and does not produce the specific intestinal lesions of human typhoid, though the poisons generated by it cause intestinal injection and diarrhœa, as do those of many other pathogenetic organisms. So that it is possible in the human subject for the symptoms of enteric fever to occur without intestinal lesions being found on post-mortem examination; and such cases have been reported. It was for a long time doubtful whether the lower animals were capable of acquiring the human form of typhoid, recently, however, Remling appears to have succeeded with rabbits and rats by giving intensely virulent cultures with the food, and so produced infiltration and ulceration of the agminate glands. It would appear, therefore, that in the human subject the bacillus is introduced by swallowing, and that the intestinal glands are primarily affected as being the seat of absorption and not secondarily as the result of a blood infection.

In man the typhoid bacillus occurs in the inflamed intestinal and mesenteric glands; in the spleen; less abundantly in the intestinal contents and the fæces; it has also been found in the liver, the bile, the urine, the blood, the cerebral meninges and ventricles, and in secondary abscesses of distant parts where it has been found still alive, even as long as seven years after the attack. It is, therefore, evident that though chiefly located at the seats of absorption it becomes more or less diffused through the system. It does not usually cause suppuration, and the secondary abscesses are mostly due to pyogenic microbes, but in some cases these abscesses have been found absolutely sterile as regards other than the typhoid organisms.

Etiology.—First to be considered are (*a*) the conditions which favour the multiplication of the bacillus and facilitate its entrance;

and, secondly, (*b*) those which affect the susceptibility of the individual.

(*a*) We may regard the bacillus either as a saprophyte which naturally lives in soil contaminated by animal matter, but which is capable of becoming parasitic when it obtains entrance into the body—a facultative parasite ; or more probably as an organism which only obtains its full development and properties in the animal body, but which can maintain an existence outside—a facultative saprophyte. It is evident that no sharply-defined line of demarcation can be drawn between these two classes, but the question is important with regard to the occurrence of apparently spontaneous or *de novo* outbreaks of the disease.

The bacillus in all probability obtains entrance into the system by being swallowed, either with the food or drink, or by putting into the mouth some contaminated object, as, for instance, a soiled finger, or by drawing into the mouth or pharynx the germs suspended in the air.

The most common cause of outbreaks of typhoid is contamination of the drinking water. This may be due to soakage of sewage or fæces into wells, sewage contamination of rivers, lakes, ponds, springs, reservoirs. Permanent infection of the soil by the typhoid bacillus may render the disease endemic in a locality, and give rise to outbreaks without any fresh importation of the poison. Faulty construction of cisterns, waste pipes, water closets, will cause localised outbreaks by contaminating the house supply.

Milk and articles of food containing or derived from milk, as butter, creams, ices, frequently spread the disease. There is no reason for supposing that the milk as passed from the cow is ever infected ; in most cases the contamination is due to the water used to wash the dairy utensils, or which has been mixed with the milk. Not only does the bacillus maintain its vitality but freely multiplies in milk. Many other articles of food which are eaten uncooked are liable to spread the disease, especially oysters cultivated in estuaries which receive sewage, water cresses grown in ditches contaminated by sewage, lettuces, and other salads watered with polluted water. It is probable that articles of food, especially in hot countries, may be contaminated by flies to whose feet the typhoid germs may easily adhere. Outbreaks of typhoid have been ascribed to eating diseased meat, but some doubt exists as to the exact nature of the disease in these outbreaks. In a recent one a specific bacillus, closely resembling but distinct from the typhoid bacillus, the *bacillus enteritidis* of Gärtner, was discovered.

Typhoid fever may also be acquired through aerial infection, by inhalation of emanations from drains, sewers, water closets, privies, dust heaps, fæcal discharges which have been allowed to dry on the patient's linen or person, or in receptacles. Probably in these cases the bacillus has become dried and disseminated as dust, but experiments have shown that a very slight current of air, 4 metres per second, will raise germs into the atmosphere from the surface of liquids or wet ground, and a current of 30 metres per second from dry surfaces. It is not, however, probable that any distant infection can take place in this manner, as free dilution with air renders the virus inert.

Direct contagion from the sick to the healthy plays but a small part in the spread of the disease. There is no reason to suppose that the poison is given off in the breath or emanations from the body, but is contained only in the fæces and to a less degree in the urine, and if these be properly disinfected and disposed of, strict cleanliness be observed, and attention be paid to the disinfection of the soiled linen, the risk of contagion may be reduced to a minimum. Nevertheless, it has not been found possible entirely to prevent the spread of the disease to the attendants. It seems probable that the alvine discharges are less virulent when first passed than after the lapse of some little time. The conditions which favour the multiplication of the bacillus and the intensification of its virulence outside the body are still imperfectly known.

The disease appears to occur in all climates, but is most prevalent in temperate and subtropical regions. In temperate climates it is especially an autumnal disease. In this country it is most prevalent during the months of September, October, November; least so in April, May, and June. A hot dry summer increases the autumnal prevalence. Great importance was attached by Pettenkofer to the height of the ground water, a low ground water coinciding with outbreaks of the disease; whether this be due to this condition favouring the contamination of the water supply, or to its facilitating soil pollution and the rising of the germs into the air is uncertain. In England this relation of the height of the ground water to outbreaks of the disease has not been observed.

(*b*) The conditions affecting the susceptibility of the individual are as follows:—

Typhoid fever occurs at all ages, but is most frequent between five and thirty-five. Exceptional cases have been met with as young as three months, and as late as seventy years. It is equally common in both sexes, and attacks persons in all ranks of life.

One attack confers immunity, though not an absolute one, against a second. New-comers into infected localities are generally considered to be more susceptible than old residents; probably these have been rendered more or less immune by repeated slight infections. In India, where the disease is extremely common and fatal among the English sojourners, especially the new-comers, the natives used to be regarded as very little susceptible, but recently the observations of Major Frazer, M.D., founded on Widal's test, tend to show that this immunity of the native population is due to a large proportion of them having been attacked in early childhood, when the disease is rarely fatal. European troops, when campaigning in tropical and subtropical climates, are very subject to typhoid, but the causes of this prevalence are still obscure.

Morbid anatomy.—Together with the lesions due to the typhoid bacillus there are usually others caused by other pathogenetic organisms, streptococci, staphylococci, etc.

The characteristic typhoid lesions are acute inflammation, usually terminating in necrosis and ulceration of the agminate and solitary glands of the small intestine, and sometimes of the solitary glands of the large bowel; inflammatory infiltration of the mesenteric glands; and parenchymatous swelling of the spleen.

The changes in the glands consist of hyperæmia, with hyperplasia and exudation of lymphoid cells. The agminate glands in this stage form raised patches of a pinkish-gray colour, with reticulated, rugose, or smooth surfaces, accordingly as the infiltration is uniform in all the tissues of the patch, or is greater in the follicles, or in the intervening tissues. This stage usually attains its maximum development in about ten days. The solitary glands present similar changes. The next stage consists of necrosis of many of the patches and solitary glands, the swollen tissues become converted into yellowish-brown sloughs, the separation of which, by a process of ulceration, occupies the third and often part of the fourth week. After the separation of the sloughs the typhoid ulcers are left. Those corresponding to the agminate glands are oval in shape, their long diameter corresponding to the direction of the intestine; they are situated on the side of the bowel opposite to the attachment of the mesentery; those corresponding to the solitary glands are circular in shape. The surface of the ulcers is smooth, their edges undermined; their depth depends on the extent of the previous inflammatory infiltration. The floor may be formed by the muscular or the peritoneal coat, or the latter may itself be involved in the sloughing process, and as the slough separates per-

foration may take place. As the ulcers heal the undermined edges become adherent to the subjacent tissues, the surface granulates, the epithelial covering is restored, and no contraction takes place. This healing process occupies an uncertain time, usually a week or ten days, but the ulcers may pass into what is termed an atonic condition and become chronic, and sometimes even extend and give rise to hæmorrhage or perforation when the patient is apparently convalescent. These changes are always most marked and most advanced in the lower part of the ileum. Sometimes the solitary glands throughout the whole course of the large intestine are similarly affected.

The mesenteric glands corresponding to the affected part of the intestine become swollen by cellular hyperplasia and exudation, and are very hyperæmic. Sometimes they soften, break down, and may burst into the peritoneal cavity; generally resolution takes place, and they get restored to their normal condition. Occasionally they become caseous, or ultimately atrophy.

The spleen becomes greatly enlarged from cellular hyperplasia and hyperæmia; it is softer and redder than in health. With the subsidence of the fever it returns to its normal condition. Both the spleen and the mesenteric glands contain the bacilli in large numbers.

There is usually more or less cloudy swelling of the secreting cells of the glandular organs.

The liver often presents interstitial deposits of leucocytes. In rare cases the gall-bladder has been found ulcerated, and even perforated.

Occasionally there is parenchymatous nephritis, more often the renal change does not go beyond cloudy swelling of the epithelium.

The heart is often softened, the muscular fibres granular, or even fatty, and the striation obscured.

There is usually hypostatic congestion of the lungs; sometimes lobular or lobar pneumonia. Occasionally there are deep ulcers in the larynx, usually on the posterior surface between the vocal cords, but the epiglottis and the mucous membrane covering the arytænoid cartilages may be affected; these ulcers may extend to and cause necrosis of the cartilages.

Many of the voluntary muscles, especially the recti abdominis and the adductors of the thigh, often show the changes termed Zenker's vitreous degeneration, or myositis typhosa, though they are not peculiar to typhoid fever. The muscular fibres undergo coagulation necrosis; they swell up, lose their striation, become homogeneous,

so as to resemble cylinders of wax, and then break up into fragments by transverse fissures and are absorbed; at the same time there is an interstitial exudation of leucocytes. If recovery takes place the fibres are regenerated by a cell growth within the tube of sarcolemma. Sometimes this process is accompanied by hæmorrhage into the muscle.

Other secondary inflammations and degenerations may occur. Superficial osteitis causing subperiosteal suppuration is not very infrequent; abscesses may form in various parts; venous thrombosis, peripheral neuritis, degenerations of the spinal cord, but none of these are special to typhoid fever.

Incubation.—The usual period of latency or incubation after infection varies from ten to fourteen days, but it may be as short as five, or as long as twenty-one days, or even longer. Usually this period is free from symptoms; sometimes there is some degree of malaise present, which may gradually deepen and pass into the febrile stage. Occasionally at the commencement there is diarrhœa, and sometimes, especially in children, vomiting, these symptoms subsiding after a few days.

Symptoms and course.—The *onset* of the disease is often somewhat insidious, the patient feels chilly, complains of languor and weariness, suffers from headache and pains in the limbs, passes restless nights with sleep disturbed by dreams, the tongue is coated, red at the tip and edges. Frequently there is slight bronchitis. The temperature rises gradually, often by regular gradations, a degree or more every successive night, the morning temperature being a degree lower than the evening one. These symptoms sometimes continue five or six days before the patient is compelled by increasing debility to take to his bed. In other cases the onset is more sudden; there are initial rigors, severe headache and pains in the back and limbs, with rapidly increasing prostration, so that the patient has to lie up at once.

By the *end of the first week* the *characteristic symptoms* of the disease are usually well marked. The patient has a depressed languid aspect; he complains of headache, thirst and general malaise; the cheeks often show a circumscribed pink flush; the pupils are somewhat dilated, but there is no injection of the sclerotics so often present in typhus. The lips are dry and parched, often desquamating; the *tongue* coated on the dorsum with a white fur, red at the tip and edges. In most cases the *bowels* are relaxed, two to four loose light yellow motions, resembling pea-soup, are passed daily, but not unfrequently there is constipation, and the

motions are solid. The *abdomen* is usually somewhat distended; often there is gurgling on palpation in the right iliac fossa. On percussion the *spleen* is found to be enlarged, perhaps measuring five inches in the vertical line, but not usually projecting below the costal arch. The *pulse* varies from 100 to 120; it is moderately full but very compressible, the arterial tone being low. Often drawing the back of the finger across the skin of the trunk produces a well-marked red *tache* with a pale border. The *temperature* varies from 102° to 104° at night, and is a degree or less in the morning, but it is very labile, *i.e.* easily affected by transient conditions. The *skin* is dry, but occasional perspirations are not infrequent. Sometimes there is a slight general febrile blush, and as the throat is often dry and a little reddened, and the tongue also red, a suspicion of scarlatina may be excited. Occasionally there is epistaxis, which may be very profuse and occur at any period of the fever.

The characteristic *rash* of typhoid usually makes its appearance between the seventh and twelfth days, but may be seen as early as the fifth, or delayed till the fourteenth day or later. The rash consists of slightly elevated circular papules of a rose colour, which disappear with pressure and reappear when the pressure is removed; their number varies greatly; there may be only three or four visible on the abdomen, or they may be thickly scattered over the trunk and extend to the limbs, and in rare cases they are seen on the face. They have a circular outline, and are regular in form, measuring two or three lines in diameter. When the rash is very intense, they may be darker in colour and persist on pressure, owing to some effusion of the colouring matter of the blood, but they never become converted into petechiæ. Occasionally a minute vesicle forms on them. They are developed in successive crops, each spot lasting three or four days, and the total duration of the eruption is usually from ten to twenty-one days, less in children, but they may continue to come out during convalescence, and usually recur when a relapse takes place. The rash is not invariably present, especially before the age of ten or after that of thirty. There is no necessary connection between the amount of the rash and the severity of the attack.

Pale bluish spots are occasionably visible, which are not raised and do disappear on pressure, the *tache bleuâtre* of Trousseau. Their most frequent seat is the abdomen and thighs; they have been attributed to lice, but are not necessarily associated with them.

Sometimes, as in other infectious fevers, the disease assumes a

hæmorrhagic form and purpuric spots appear on the skin, and there may be hæmorrhages from the mucous membranes. Though the prognosis in these cases is unfavourable, nevertheless recovery may take place.

The *urine* presents the usual characters of febrile urine: it is concentrated, diminished in quantity and of high specific gravity; it contains an excess of urea and uric acid, and of the sulphates and potassium salts, and a diminished amount of sodium chloride. In severe cases it is often albuminous.

Ehrlich's test—Diazobenzol reaction.—In a large proportion of cases this reaction is present, and is not without value as a diagnostic sign. Two solutions called *A* and *B* are prepared. *A* consists of a 20 per cent solution of hydrochloric acid saturated with sulphanilic acid. *B*, of a half per cent solution of sodium nitrite. Immediately before using, one part of *B* is mixed with twenty-five parts of *A*, an equal volume of urine is added in a test-tube and strong liquor ammonia is dropped into the mixture or allowed to flow down the side of the tube. At the junction a crimson ring forms; if the tube be shaken the froth is coloured pink; ordinary urine gives a more or less deep orange colour. In applying the test care should be taken to mix the solutions accurately. The reaction is seldom absent in typhoid, even in mild cases, and is valuable as a negative test; it is, however, occasionally present in other diseases, especially measles, pneumonia, tuberculosis. Liquid cultivations of the typhoid bacillus are said to give it.

The urine in typhoid fever possesses highly toxic properties, and the typhoid bacillus appears to be usually present in it.

The *blood* in the later stages of typhoid shows important changes. The red cells and the hæmoglobin are much diminished; the leucocytes are also usually rather decreased in number, though only slightly; these changes are most marked in the third and fourth weeks. Secondary inflammations will cause an increase in the leucocytes. This absence of leucocytosis in typhoid may have a diagnostic value and help to distinguish it from inflammatory and septicæmic fevers.

During the *second and third weeks* the symptoms become more severe, the prostration increases, there is rapid wasting, the tongue often becomes denuded, red, glazed and transversely fissured, the lips are dry and cracked; often there are sordes on the teeth. The pulse becomes dicrotic from loss of arterial tone; it may vary in frequency from 112 to 140; if persistently above 120 it is an unfavourable sign. The first sound of the heart becomes altered in

quality, becoming short, more like that of the second. Signs of hypostatic congestion of the lungs may appear, increased frequency of breathing, duskiness of the countenance, crepitations over the back of the chest. Delirium is not infrequent, at first on waking out of sleep; it is usually of a quiet muttering character, sometimes noisy and violent. In very severe cases the patient may pass into what is called the "*typhoid state*"; there is delirium with stupor, great prostration, the patient sinking down in the bed, and subsultus tendinum; the urine and motions are passed in the bed, or the bladder may be paralysed. Bed-sores are liable to form. The patient may die in a state of coma. These severe symptoms are only occasionally present.

During the third week the *diarrhœa* usually becomes more severe; there may be six or eight motions in the twenty-four hours; they are often very offensive, alkaline, and may contain shreddy sloughs. Hæmorrhage, slight or profuse, is liable to occur, or perforation.

The *temperature* during the third week becomes more remittent in type, and towards the end or the beginning of the fourth begins to fall, the morning temperature falling more rapidly than the evening. It is, however, by no means unusual for the temperature to keep up during the first part or the whole of the fourth week, or even longer. In favourable cases, during the fourth week defervescence is completed, and the temperature usually remains subnormal for some time, but is easily sent up by slight causes; the appetite returns, often before the temperature has fallen to normal, and convalescence is established, though liable to be interrupted by many accidents.

Typhoid fever presents great variations in its characters and severity, and many forms are described, which, however, are not distinguished by any strict line of demarcation. Considerable difference has been noted in the prevalence of certain symptoms in various epidemics. In some the symptoms due to the blood-poisoning are predominant, in others those caused by the local lesions.

Among the more common forms are:—

1. The acute form.—This is characterised by sudden onset, severe febrile symptoms from the first, rigors, rapid rise of temperature, headache, oppression, early delirium, and death may take place, though this is very exceptional, during the second week. The intestinal lesions are not necessarily excessive, and the later stages of the fever may be less severe.

2. The abortive form.—Here the earlier symptoms may be

severe, but sometime between the eighth and fourteenth days a rapid defervescence takes place. Probably in these cases the intestinal lesions are slight and have not gone on to the sloughing stage.

3. The latent or ambulant form.—Here the general febrile disturbance is comparatively slight, but the intestinal lesions present the usual characters. In consequence the patient continues to follow his usual avocation and walks about during the whole or a great part of his illness, though suffering from malaise and diarrhœa. The neglect of proper precautions renders these cases very liable to hæmorrhage and perforation.

4. The afebrile form.—Cases have been observed where the temperature has remained normal or subnormal throughout the attack. This has been especially noticed where there had been previously exposure to great hardships.

Mild forms of typhoid are often called febricula, gastric fever, bilious fever, simple continued fever, remittent fever, but these terms should be avoided as much as possible.

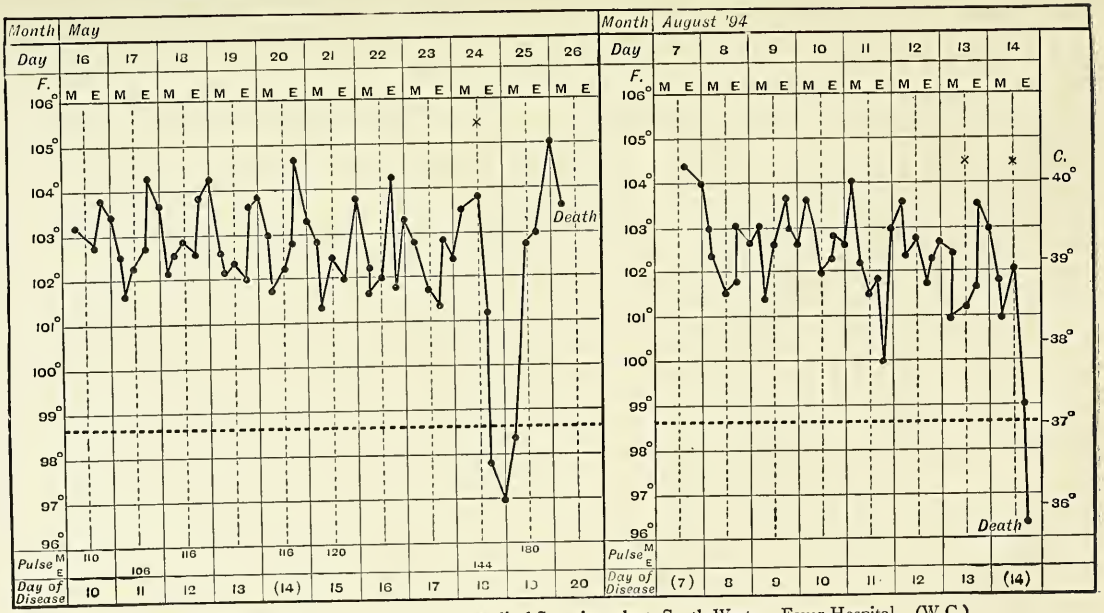
Complications and sequelæ.—Of the complications of typhoid fever those due to the intestinal lesions are the most important, and of these the most serious are hæmorrhage and perforation. They may occur at two periods, most commonly during the separation of the sloughs in the latter half of the third or the first half of the fourth week. But they may take place much later, during the stage of convalescence, in consequence of the ulcers not having healed. *Hæmorrhage* occurs in about 6 per cent of the cases; the amount may vary from a slight oozing to several pints of arterial blood. The blood may be either dark or bright red according to the time it has remained in the bowel before being evacuated, and is often clotted. When profuse it causes a sudden fall of temperature, pallor, and collapse; it may be repeated several times. A moderate hæmorrhage does not exercise any injurious effect on the course of the disease, but indicates deep ulceration. A profuse hæmorrhage may be immediately fatal. Hæmorrhage as well as perforation may occur when the bowels have been previously constipated.

Perforation has been estimated to occur in about 3 per cent of all cases. It manifests itself by sudden pain in one part of the abdomen, followed by signs of general peritonitis, diffused abdominal pain, tenderness, distention, and collapse. The temperature often falls and then again rises. The pulse is very frequent and small, the countenance pinched; there is often hiccough and vomiting. Death

Temperature Curves in Two Fatal Cases of Typhoid Fever.

I. Perforation on 18th Day.

II. Hæmorrhage on 14th Day.



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usually occurs from within twenty-four to forty-eight hours. Sometimes when the patient is in a typhoid state these severe symptoms are absent, and the chief indications are great distention with increased prostration and some abdominal tenderness. The abdominal distention is usually due mainly to inflation of the intestine, but sometimes considerable quantities of gas escape into the peritoneal cavity and cause obliteration of the liver dulness, an important diagnostic sign. Perforation and peritonitis cause a great increase in the number of leucocytes in the blood. Recovery may take place after symptoms of acute peritonitis have occurred; possibly in these cases there has not been actual perforation, or extravasation has been prevented or limited by adhesions. Peritonitis may also be caused by the breaking down and rupture into the peritoneal cavity of the infiltrated mesenteric glands.

Ulceration of colon.—Occasionally the solitary glands throughout the colon and rectum are affected in a similar manner to those of the ileum, and the whole of the large bowel riddled with circular sloughing ulcers. This condition is one of great gravity, and is manifested by the severity and long persistence of the diarrhœa, the highly offensive motions, which often contain mucus, and by the pain and sometimes the tenesmus which accompany them. There may be distinct tenderness along the course of the colon. Hæmorrhage and perforation are liable to occur.

Gastric disturbance.—Severe gastric disturbance occasionally occurs; there is flatulent distention, sometimes acute dilatation and frequent bilious vomiting, so that the patient can retain no food. These symptoms are often associated with severe headache. The term bilious typhoid has been applied to this form.

Jaundice occasionally occurs in the later stages of the disease and the case often terminates fatally, the motions remaining bile-stained. Its pathology is not certainly known. The liver is often found to be fatty with exudation of leucocytes between the lobules.

Tympanites.—This, when great, is both a distressing and dangerous symptom. When it occurs early it is an indication of great nervous depression; later it is usually associated with extensive ulceration, or it may be a sign of peritonitis. The distention may affect both the large and small intestine. It tends to embarrass the patient's respiration, and increases the risk of perforation by stretching the intestinal wall.

Respiratory complications.—Some degree of bronchitis is usually present. In severe cases, in the later stages there is often hypostatic congestion of the lungs due to weakness of the heart, and favoured

by the dorsal decubitus of the patient. It is manifested by frequent shallow breathing and some duskiness of countenance; the physical signs are some degree of impairment of resonance over the back, with rather fine crepitant râles.

Lobar pneumonia is an occasional complication. It is most common in the third or fourth week of the disease, and is due to invasion by the pneumococcus, and not to the direct action of the typhoid bacillus. Occasionally it occurs at the outset, and is possibly due to a primary infection of the lung, the intestinal symptoms developing later. Cases of pneumonia have been met with during an epidemic in persons who have been exposed to the contagion without any other symptoms of typhoid developing. When it occurs late in the disease many of the usual symptoms may be absent; there is often little cough and no expectoration, but the breathing is quickened, the countenance dusky, the alæ nasi often dilate, and there may be pain in the side. Though a very serious complication, it is not necessarily fatal.

Embolic and pyæmic processes in the lungs are liable to occur, and may give rise to abscess, empyema, or pneumothorax.

Ulceration of the larynx, originating in the lymph follicles, is not infrequent; often it gives rise to few symptoms, in other cases there is huskiness or stridor of the voice and cough, pain in swallowing, and tenderness, on pressure, over the larynx. Generally the ulcers heal without causing any serious mischief. They may, however, extend deeply, and cause necrosis of the cartilages, œdema, and stenosis of the glottis, and necessitate tracheotomy; sometimes they cause profuse hæmorrhage.

Cardiac complications.—Endo- or pericarditis are rarely met with, but in severe cases the muscular wall is softened and the cavities dilated. This condition is indicated by a short, rather sharp, first sound, feeble impulse, and perhaps slight extension of the area of cardiac dulness. Sometimes there is a systolic apex murmur due to the dilatation and to the weakening of the musculi papillares. When recovery takes place, the heart usually returns to its normal condition. Sometimes sudden death occurs during convalescence, probably due to this condition of the heart. Thrombosis of the cavities of the heart or pulmonary artery may occur from stagnation of the circulation.

Thrombosis of the veins, chiefly the saphena, the femoral, and the iliac veins, often occurs during convalescence. It may begin in the intramuscular veins as the result of the myositis typhosa, and extend to the larger veins. Generally, in a variable time, from three to six

weeks, the thrombus gets absorbed, and the calibre of the vein is restored. Sometimes the obstruction remains permanent; occasionally it gives rise to pulmonary embolism. The affection is marked by swelling of the leg, pain, and tenderness along the course of the affected vein, which can often be felt as a hard cord.

Renal complications.—Albumen is often present in the urine in severe cases, but disappears as defervescence takes place. Occasionally acute tubular nephritis occurs, characterised by scanty, bloody, highly albuminous urine, containing epithelial casts. There may be dropsy and uræmic symptoms. The term nephrotyphoid has been given to these cases.

Nervous complications.—Various disturbances of the nervous system may occur during and after the attack. The headache, delirium, subsultus, and floccitatio or picking at the bedclothes, of severe cases are not accompanied by any appreciable lesions of the nerve centres, and are probably toxic in their nature. Sometimes spasmodic and convulsive affections, as retraction of the head, rigidity of the trunk or limbs, strabismus, trismus, take place, without any lesion being detected.

Meningitis is a rare complication, and is usually of septic origin; but in some cases the typhoid bacillus has been found in the exudation. Thrombosis and embolism of the cerebral arteries may occur, and cause hemiplegia and aphasia, which are usually recovered from.

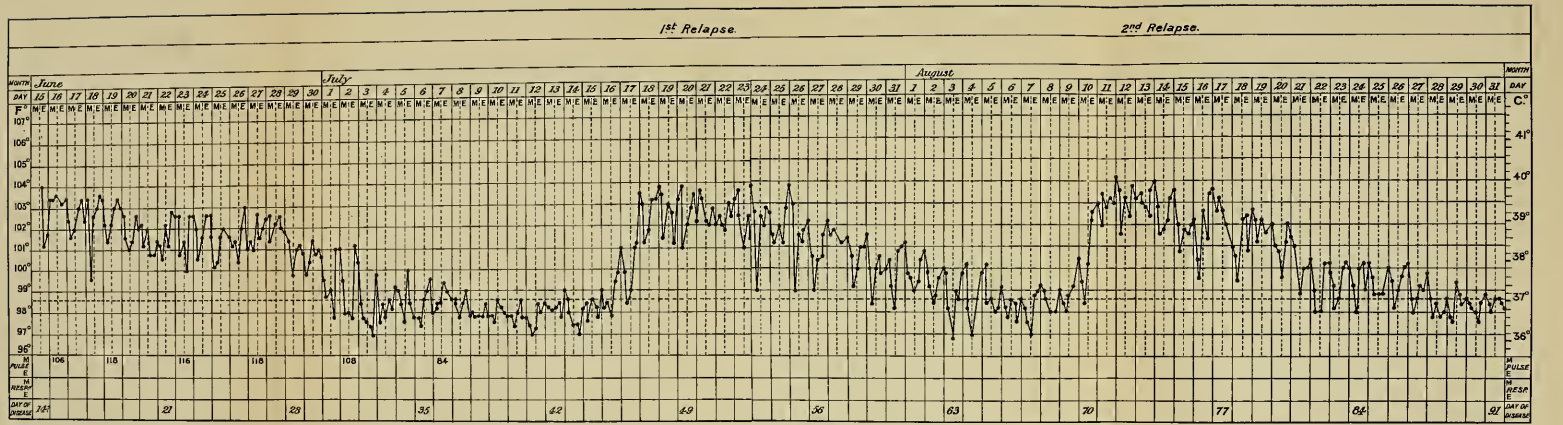
Peripheral neuritis affecting the nerves of the extremities sometimes manifests itself during convalescence. Pain, tenderness, loss of power, numbness, and tingling, are observed. A common seat is the ulnar nerve, causing numbness, tingling, and loss of sensation in the little and ring fingers; this is probably due to pressure on the nerve behind the condyle of the humerus, from the arm being constantly kept in one position owing to the apathy of the patient. Extreme tenderness of the toes may occur, lasting a week or ten days, probably due to peripheral neuritis. The symptoms in some cases suggest the possible implication of the vagus.

Another extremely painful affection during convalescence, which is probably of a neuralgic nature, has been termed the typhoid spine. There is extreme pain over the lower part of the back and the sacral region, especially on movement; moving the legs also causes great pain. There is no paralysis, or alteration of the electrical reactions. The condition may last for several weeks.

Occasionally serious lesions of the spinal cord have followed typhoid, as poliomyelitis, and disseminated sclerosis.

Melancholia, dementia, and sometimes mania, are liable to follow

Temperature Curve in a Case of Typhoid Fever—Two Relapses—Recovery.



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typhoid. They are generally only temporary, but may necessitate putting the patient under restraint.

Organs of special sense: a temporary deafness is often present during the attack; occasionally a suppurative otitis media occurs. Double optic neuritis may be present, without there being any intracranial disease.

Recurrent rigors are sometimes observed during the attack, without any suppuration following. Occasionally, however, pyæmia occurs. More frequently external suppurations manifest themselves, often during convalescence; among these is a suppurative parotitis, the gland probably getting infected by germs entering from the mouth through the duct.

Sometimes there is a *superficial suppurative osteitis* affecting especially the ribs, femur, and tibia. The typhoid bacillus has been discovered in the pus of these abscesses. Sometimes the affection has a rheumatic character; there are aching pains, especially at night, swelling of the epiphyses with irregular fever, and the affection may last for weeks without suppuration taking place.

Relapses are very common; their frequency has been estimated at 5 to 10 per cent. Most commonly the relapse takes place within fourteen days after defervescence, but the interval has been known to be as long as ten weeks. In the relapse all the symptoms recur, and the rose spots come out again, and fresh infiltration and ulceration of the intestinal glands takes place. Most commonly, but by no means always, the relapse runs a shorter course than the primary attack. The fever attains its maximum between the fourth and sixth days, and defervescence begins before the end of the second week; but the attack may last the usual time. A second, and even a third, relapse may take place. Relapses are often attributed to errors of diet during convalescence, but they frequently occur when all precautions have been strictly observed. Besides these relapses after defervescence, intercurrent relapses, or recrudescences, may take place before the temperature has become normal; they are indicated by an exacerbation of the febrile symptoms and the appearance of a fresh crop of rose spots. In this way an attack of typhoid may be indefinitely prolonged.

Desquamation of the cuticle sometimes takes place after typhoid. Occasionally the hair falls out; the nails may show a transverse groove, indicating cessation of growth during the attack.

A condition of *marasmus* may follow, due, possibly, to atrophy of the mesenteric glands.

Pregnant women very commonly, but not always, miscarry.

The child, if near the full time, may be born alive and healthy; but it has been found infected with typhoid bacilli in the blood and spleen.

Diagnosis.—The chief points to be noted in the diagnosis of typhoid fever are: the rose spots, the diarrhœa, the enlarged spleen, the tumid abdomen, the characters of the tongue, and the duration and course of the fever. In temperate countries, a fever which lasts a week without the appearance of any characteristic rash, or any local inflammation, is almost always typhoid.

To these points must be added the diazobenzol reaction of the urine, and **Widal's serum test.** This last depends on the fact that the blood serum of persons suffering from typhoid, or who have been rendered immune by a previous attack, impairs the vitality of the typhoid bacilli, and causes them, when cultivated in a liquid medium, to clump together and become motionless. In applying Widal's test the points to be especially observed are—first, to use only a fresh bouillon culture, as the typhoid bacillus rapidly loses its potency. Secondly, to dilute the serum or adjust its proportion to the culture, as the clumping action may be produced by healthy serum if too concentrated; the proportion must not exceed one drop of serum to ten drops of the culture; in the second week of typhoid 1 to 100 is often sufficient. Thirdly, to note the time required to effect the clumping; this should not exceed half an hour, often a few seconds are sufficient; healthy serum may produce the reaction in the course of a few hours (see p. 33).

The most convenient method of procedure is as follows:—The lobe of the ear should be punctured and a little blood squeezed out into a small tube, or sucked out by means of a capillary pipette and expelled into the tube. It should be allowed to coagulate, and by means of a platinum loop a drop of the serum added to 10, or, better, 20 or even 30 drops of the culture and examined at once under the microscope between a cover-glass and slide. The proportion of 1 to 10 is open to many fallacies. The blood as drawn may be used, but the corpuscles are apt to obscure the microscopical appearances. No antiseptic precautions are necessary, as there is not time for other organisms to grow. Dried blood or dried serum can be employed after dissolving in water, but it is difficult to estimate the degree of dilution. If the blood has to be sent away for examination it should be withdrawn with antiseptic precautions and sealed up in a capillary tube furnished with a bulb. The reaction may usually be obtained by the seventh day, and has been found as early as the fifth; but its appearance may be delayed till

a much later period, even as late as the twentieth day. It may continue for a few days after convalescence to many years, or possibly the remainder of the patient's life. It may be temporarily absent and appear again, so that if a negative result is obtained it is necessary to repeat the test several times. On the whole, it may be said that the presence of the reaction in a person who has not had a previous attack is an almost certain indication of the disease; but its absence on any given occasion does not necessarily exclude it.

In certain cases, exhibiting all the clinical features of typhoid fever, when the Widal reaction has been wanting, the B. typhosus has not been found, but another organism differing both in morphological and cultural characters from the typhoid microbe and from B. coli.

The diseases with which typhoid is most likely to be confounded are, first, *acute tuberculous affections*, especially meningitis, general miliary tuberculosis, and tuberculous affections of the abdominal viscera.

In tuberculous meningitis vomiting is a more prominent symptom. The abdomen is usually retracted instead of being tumid; the bowels are commonly constipated; the tongue is not red; the spleen is not enlarged; the pulse is often infrequent; the temperature is more irregular; the tache cérébrale better marked. The knee jerk is often absent, whereas in typhoid it is often exaggerated. Later on there may be the hydrocephalic cry, spasm, or paralysis of the cerebral nerves; but it must be remembered that in typhoid there may be inequality of the pupils, strabismus, twitching of the muscles, double optic neuritis. "Stocker's symptom" is of some value; in typhoid, if the bedclothes be pulled down the child is indifferent, but in tuberculous meningitis he resists and immediately draws them up again. In typhoid the decubitus is usually dorsal, in meningitis lateral. The presence of tubercles in the choroid would be a valuable diagnostic sign.

In acute miliary tuberculosis the pulmonary symptoms are usually much more severe than in the early stage of typhoid. There is usually great rapidity of the breathing; the alæ nasi dilate; the face is somewhat cyanosed; fine crepitant râles are audible over the chest; the temperature is much more irregular, and may be of the inverse type, *i.e.* higher in the morning than in the evening. If there is also tuberculosis of the intestine, there may be diarrhœa, and a swollen abdomen.

Tuberculous peritonitis may resemble typhoid, but is usually much more chronic, and often there are signs of peritoneal effusion.

Pneumonia of the asthenic type may closely resemble typhoid, but may be distinguished by the physical signs. When it occurs as a complication of typhoid, other symptoms must be looked to—the rose spots, the enlarged spleen, the diarrhœa, etc. Most commonly pneumonia occurs in the later stages of typhoid, so that the duration of the attack will have been longer than is usual in primary pneumonia.

The *fever which accompanies appendicitis and perityphlitis* often resembles typhoid, but the local pain, tenderness, and swelling will serve to distinguish them.

Typhoid fever is very liable to be mistaken at the onset for *influenza*. The invasion of the latter is usually more sudden, and the early symptoms more severe. The temperature reaches its maximum much sooner. The pains in the head and limbs are more intense, and of a more neuralgic character; and unless some local complication interferes, defervescence takes place in the course of a few days. If the fever persists without any local cause, the case is probably typhoid.

Ulcerative endocarditis and pyæmia may closely resemble typhoid, and the former may even cause intestinal hæmorrhage from embolism. The greater irregularity of the temperature, the signs of embolism, as purpuric spots and blotches on the skin, hæmaturia, and the cardiac signs, are the chief points of distinction.

In children *acute gastric and intestinal catarrh* may simulate the milder forms of typhoid; but the febrile disturbance is of shorter duration, the spleen is not enlarged, and there are no spots. A suitable purge will often remove the symptoms.

In tropical climates, in malarial districts, there may be great difficulty in distinguishing *malarial remittents* from typhoid, and no doubt both infections may be present together.

For the diagnosis from typhus, see the latter disease.

Prognosis.—The rate of mortality of typhoid fever varies so much in different epidemics and under different modes of treatment, that it is impossible to give any average generally applicable. In the general hospitals of London it is about 16 per cent; in the Fever Hospitals of the Metropolitan Asylums Board somewhat higher; in private practice probably less, and often much less in extensive epidemics.

It is claimed that systematic cold bathing will reduce the hospital mortality to less than half that given above. An equally great reduction is claimed by the advocates of the antiseptic treatment.

Age.—The influence of age in the rate of mortality of typhoid is much less than in typhus, but the mortality in childhood is less than in adult life, and after thirty-five is decidedly higher than below that age. *Sex.*—The mortality of females is slightly higher than that of males. *Bodily habit.*—Great obesity and also great muscular development are unfavourable.

Antecedent and general conditions.—Intemperate habits, too high living, organic disease, as of the heart or kidneys, delay in the commencement of treatment, increase the rate of mortality. It has often been observed that among the Irish, who are comparatively ill-fed and live largely on potatoes, the rate of mortality is very low.

Unfavourable symptoms.—The more important among these are indications of severe intestinal lesions, as urgent diarrhœa, hæmorrhage, abdominal pain, great tympanites, disturbance of the nervous system, as muttering delirium, tendency to stupor, muscular twitchings, a pulse persistently above 120, indications of heart failure, hypostatic congestion of the lungs, a persistent high temperature, especially if accompanied by disturbance of the nervous system. Mere temporary rises of temperature are of comparatively little moment.

Prophylaxis of typhoid.—This is mainly a question of public hygiene and sanitation, to ensure that the water supply is not contaminated by sewage; that the sanitary arrangements are in good order and do not allow the emanations from drains and soil pipes to escape into houses and foul the cisterns; to prevent the contamination of milk and shell fish, and other articles of food. If there is any reason to suspect contamination, milk and water should be boiled.

To prevent the spread of contagion from individual cases, the following precautions should be followed:—The room should be kept well ventilated, and abundant cubic space should be allowed, 1500 cubic feet if possible. The strictest cleanliness should be observed. After handling the patient, the attendants should dip their hands in an antiseptic solution, as hydrarg. perchlor. 1 to 1000, a basin of which should be placed on a table near the bed. If the hands get soiled, they should be washed with carbolic acid soap. After every motion the parts should be sponged or wiped with some antiseptic lotion, as weak condy or carbolic acid. Soiled linen should be steeped in some disinfecting solution before being sent to the laundry.

The disposal of the excreta is a matter of much importance, as it is by them that the disease is chiefly spread. The safest way of dealing with them—but this is seldom practicable—is to burn them;

they may be mixed with sawdust, oil of turpentine or naphtha poured over them, and set on fire. Under ordinary circumstances they should be disinfected before being thrown down drains or buried, by being mixed with crude carbolic acid, or perchloride of mercury, or some other disinfectant, and allowed to stand for an hour or two. The urine, also, should be disinfected. Earth closets are not suitable for typhoid evacuations.

The nurses should not eat or drink in the sick-room, and never without washing their hands.

Protective inoculation and serum treatment.—Inoculation of living or sterilised cultures of the typhoid bacillus renders animals immune against the action of the typhoid bacillus and its toxines, and the serum of animals thus rendered immune confers immunity when injected subcutaneously. According to Pfeiffer the action of such serum is rather bactericidal than antitoxic, and this militates against its curative powers.

Sterilised cultures may be employed as a protective vaccine, and the serum of immunised animals as a curative agent. The subject is still in the experimental stage, but the evidence for the preventive action of the vaccine is much stronger than that for the curative action of the serum, which latter must be regarded as still unproved. The inoculation of sterilised cultures appears to be free from risk, and deserves trial during epidemics and in the case of persons like nurses who are especially exposed to infection.

Treatment.—As soon as the diagnosis of typhoid becomes probable, the patient should be strictly confined to bed, and should pass his evacuations in a bed pan and urine glass. The room should be kept cool; the temperature should, if possible, not exceed 60°. The bed should be narrow, with an elastic mattress, and a waterproof cloth under the sheet. He should be lightly covered with a sheet and thin coverlet, with a blanket over his feet. The diet should be liquid, administered at regular intervals every four hours, or oftener if there is much prostration, and he should have abundance of drink given him to assist elimination through the kidneys. It should be remembered that the digestive and assimilating powers are much impaired; it is not therefore advisable to overtask them by an excess of food. The chief articles of food employed are milk, two to three pints of which may be given in twenty-four hours, together with animal broths and solutions of meat; ordinarily about a pint of beef tea may be given; beaten-up eggs, or egg albumen mixed with water, thin gruel and arrowroot may be administered. Plain water, barley water, acidulated drinks, weak tea,

which last is an excellent diuretic, may be allowed in small quantities at a time, according to the patient's liking. It is also advisable to give an ounce of glucose daily to supply the liver with glycogen, which under ordinary diets disappears from the liver cells in septic fevers, but which may be restored by administering glucose, and so the wasting may be diminished. It may be used to sweeten milk, tea, arrowroot, acid drinks.

When the patient is fed largely on milk the motions should be carefully inspected to see that they do not contain curds; if this is the case the amount of milk must be diminished, or it must be given diluted with barley water or lime water, or it may be peptonised, or humanised milk substituted.

In severe cases, when signs of prostration show themselves,—a dicrotic pulse, weak action of the heart, congestion of the lungs, delirium, tremors,—alcoholic stimulants should be freely administered, and it is better to anticipate rather than to defer their use. Brandy is perhaps the one most to be relied on, but the patient's predilections, if he has any, may be deferred to. The amount must depend on the age and condition and previous habits of the patient, and the effect produced. Young subjects require less than older persons. From three to eight ounces or more of brandy are often required in twenty-four hours.

To combat the disease three chief methods are employed, which may be termed the antipyretic, the antiseptic and the eliminative. The first consists in keeping the temperature through the whole course of the disease below a moderate fever height. The most effectual method of doing this, and the one which gives the best results, is by bathing the patient in tepid water. Whenever the temperature rises above 102.5° Fahr., he should be lifted into a bath of a temperature of 80° Fahr. and kept immersed for about fifteen minutes, or till shivering sets in. In some cases baths of a lower temperature may be employed or the temperature of the water cooled by ice after the patient's immersion. The temperature will continue to fall for some time after removal from the bath. When taken out the patient should be laid on a blanket, wiped dry, and lightly covered; a little alcohol should be given before the bath. Wherever this mode of treatment has been systematically carried out it has always been found to effect a great decrease in the rate of mortality. The good effects produced are by no means confined to the lowering of the temperature. The pulse is reduced in frequency, its tone is improved, the respirations are deepened, headache, delirium, insomnia, subsultus, are prevented or relieved, the amount of the

urine is increased, and its toxicity during the fever period is greatly intensified, while in the stage of convalescence it is diminished, showing that this mode of treatment is powerfully eliminative, and it is probable that this is one of its chief advantages. Hæmorrhage and peritonitis, but not congestion of the lungs, contra-indicate bathing.

Where bathing cannot be employed recourse may be had to cold sponging; sometimes where there is much collapse and cold sponging is greatly objected to by the patient, sponging with very hot water, 110° Fahr., and afterwards leaving the patient lightly covered, will bring down the temperature. Packing in a wet sheet or applying iced compresses to the chest and abdomen are also useful means. Another method is to put a cradle, merely covered by a sheet, over the patient, inside which may be placed trays of ice, and so keeping him in a bath of cool air. Many drugs have the effect of reducing temperature; the most important are quinine in large doses, antipyrine, acetanilide, phenacetine, but their use for this purpose, except an occasional dose, which sometimes produces good effects, is not to be recommended owing to their depressing action on the heart. Quinine in smaller doses may be given with advantage in the later stages of the disease.

The antiseptic treatment consists in administering remedies to destroy or render inert the typhoid and septic microbes in the intestinal canal. A large number of such remedies have been employed, among them calomel, perchloride of mercury, iodine, carbolic acid and the sulpho-carbolates, salol, β-naphthol, guaiacol, turpentine, and many others. By their use the putrefactive and fermentative changes in the intestinal canal may be arrested and the fæces deprived of their offensive smell, but no effect is produced in destroying either the saprophytic germs which are free in the intestine, or the typhoid bacilli which are lodged in the glands and spleen; these remedies have been largely used in America, and very successful results are claimed for them.

The practice has been recently revived of treating typhoid by purgatives with the object of eliminating the toxines and getting rid of the bacillus. The typhoid bacilli are, however, mainly embedded in the tissues and glands and are therefore unaffected by purgatives, and there are obvious dangers in stimulating an ulcerated bowel to active peristalsis. Many physicians, however, consider a calomel purge beneficial in the early stage of the disease.

Apart from attempts to control the general course of the disease, the special symptoms require treatment.

With regard to the bowels, it is safer not to give purgatives by the mouth after the first week or ten days. If there is constipation, enemata should be employed, as it is evidently inadvisable to leave the bowels full of putrefactive and fermenting fæces. Commonly there is diarrhœa; if the motions do not exceed three or four in the twenty-four hours no special treatment is required. If they much exceed this opium may be administered either by the mouth or as an enema, and care should be taken to adapt the diet; sometimes milk disagrees, sometimes beef tea.

If a profuse hæmorrhage occur the patient should be kept perfectly still; he should pass his motions into a draw sheet; the administration of food should be suspended for some hours. Opium should be given to arrest peristalsis, and in addition styptics may be had recourse to, though their efficacy is somewhat doubtful. The best are perhaps turpentine, acetate of lead and ergot; the last may be administered subcutaneously. If the patient appears to be in danger of sinking, transfusion of a saline solution into the veins should be resorted to.

Perforation is almost always fatal; if diagnosed early and the patient's general condition is still fairly good, the best chance is to perform laparotomy, wash out the peritoneum and close the perforation. A sufficient amount of success has now been obtained as to justify the operation in all favourable cases, and it should always be performed when perforation occurs during convalescence. If the operation is not deemed advisable opium should be administered in full doses.

For the treatment of meteorismus stimulants may be administered when there are signs of nervous prostration, together with strychnia; cold compresses may be applied to the abdomen, an enema of rue or ol. terebinth administered. Sometimes relief may be obtained by introducing a rectal tube.

Ulceration of the large intestine, which will cause the diarrhœa to persist after defervescence, requires careful regulation of the diet; acetate of lead may be given combined with opium; large doses of subnitrate of bismuth are sometimes useful.

Hypostatic congestion of the lungs and pneumonia require alcoholic stimulants, together with ammonia and ether; mustard and linseed meal may be applied, but the chest should not be blistered.

Heart failure may be treated by ether and strychnia administered hypodermically. Digitalis and ammonia may be given.

Nervous symptoms, as sleeplessness, delirium, headache, are often relieved by bringing down the temperature by bathing, sponging,

the application of cold to the head. For sleeplessness, which should never be allowed to persist, the safest drug is opium.

Thrombosis of the veins of the lower extremity should be treated by keeping the leg still by means of sandbags laid on each side, and extract of belladonna may be applied along the course of the affected vein.

Great care is required during convalescence; solid food should be resumed very gradually, and not until the temperature has been normal in the evening for several days; if there have been marked signs of ulceration, for at least a week. At first a rusk or a sponge cake may be allowed, and a piece of chocolate, which children especially eat with relish; then a lightly poached egg and a thin piece of bread and butter; next a little boiled fish; later tender meat and potatoes mashed or made into a purée. The temperature, which is usually at first subnormal, remains for a considerable time in a very unstable state, the resumption of solid food, constipation, any mental excitement will often cause a temporary febrile exacerbation; the heart too remains weak, and any strain or over-exertion may cause a fatal syncope or lead to dilatation. After an attack of typhoid the patient should always have a period of rest at a health resort or convalescent institution before resuming his ordinary mode of life.

W. Cayley.

MEDITERRANEAN FEVER

Syn. Malta, Rock or Neapolitan Fever; Undulant Fever

Definition.—An endemic pyrexial disease, occasionally prevailing as an epidemic, having a long and indefinite duration and an irregular course, with an almost invariable tendency to undulatory pyrexial relapses, and a constant occurrence in certain tissues of a definite species of micro-organism, which fulfils Koch's postulates.

Geographical distribution.—It is widely distributed in the countries bordering upon the Mediterranean, south of latitude 46° N., and along the Red Sea littoral. Analogous forms of fever, giving a serum reaction with the micrococcus of this disease, are also met with in parts of India, China, Africa, and America.

Etiology.—The disease is the result of the entrance of the *micrococcus melitensis Vel Brucii* into the tissues of the human body. This organism is constantly present in the spleens and other organs of fatal cases, can be indefinitely cultivated artificially, and is also pathogenic to monkeys.

The disease is not directly infectious from man to man. There is no evidence that it is usually disseminated by food or drink, nor has it been traced to inoculation by insects or otherwise. There is, however, a close connection between the occurrence of the disease and pollution of the soil in or around dwelling rooms or under tents, with the fæces or urine of patients suffering from this fever.

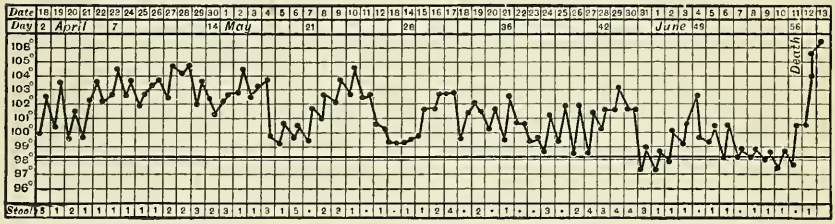
Its prevalence in the Mediterranean coasts is in exact inverse proportion to the amount and continuance of the rainfall, and in direct proportion to the average air temperature above 60° F. The disease attacks all ages, but more especially those between ten and thirty, who have not previously suffered from it. Sex, length of residence, and station in life, have apparently only an indirect influence on its prevalence. The initial symptoms, the above facts and other circumstantial evidence, lead one to suspect that the virus usually enters the body by the inspired air, and leaves it by way of the fæces (and urine?). Though not present in clean soil, the micrococcus seems able to live as a saprophyte in fæcally polluted soil. It is not supposed that the virus is carried far through the air, a distance of from 3 to 10 feet being sufficient to account for the majority of the cases.

The **incubation period** is probably between three and ten days.

Symptoms.—The writer has, for convenience, divided over a thousand cases he had treated into three clinical types, indicative of variations in severity of the fever, one type often passing into another. In the *malignant type* the onset is almost sudden; the patient complains of severe headache, "pains all over him," nausea or even vomiting, his tongue being foul, coated and swollen, and his breath soon becoming very offensive. The temperature reaches 104° or 105° and remains more or less continuously high. Diarrhœa, with most offensive stools, may be present. After a few days in this condition the patient passes into the "typhoid state," the lungs become choked, the pulse weak, and hyperpyrexia and death ensue. The bodies of such fatal cases are often most offensive and described as "rotten." In these days of energetic treatment such cases are happily rare.

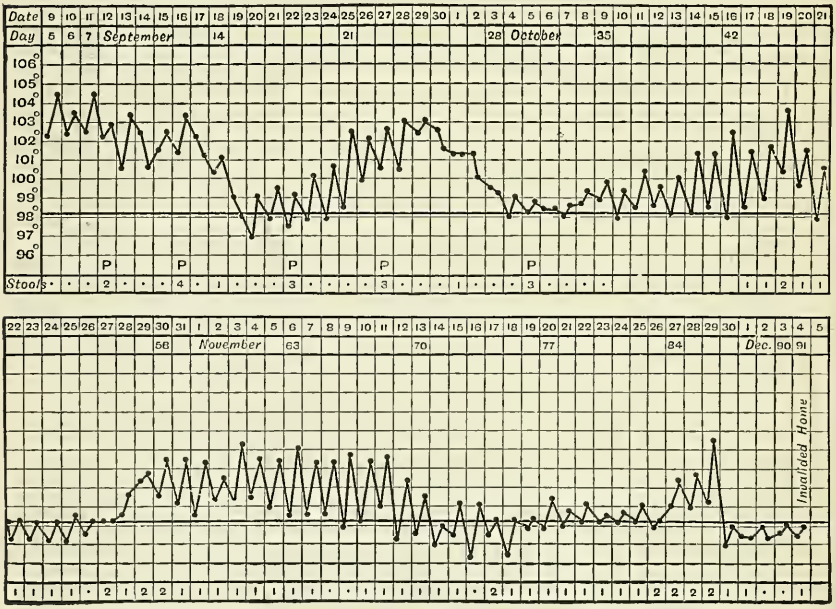
Temperature Curves in Two Cases of Mediterranean Fever.

Case I.



Short irregular pyrexial waves, with death during a relapse

Case II.



Undulatory type with well-marked waves.

In the *undulatory type* the case usually commences like one of enteric fever with constipation, followed by numerous relapses. It is thus marked by a series of waves or undulations of remittent pyrexia, separated by periods of abatement or absence of symptoms. At any stage the case may take a malignant and fatal turn, or the pyrexia may gradually subside into a daily intermittence before convalescence. The pyrexial curves average 10 days, the primary one being usually the longest (18-23 days), there being from one to seven waves in an attack. This is the commonest type of the fever.

In the *intermittent type* the temperature usually falls daily between midnight and 2 A.M. to or below normal, accompanied by profuse diaphoresis, rising slowly but steadily about 11 A.M. next day to varying heights, without rigor. This type much resembles the hectic pyrexial curve of phthisis or other suppuration. If the maximum temperatures be accurately recorded each day, they will be found to form undulations similar to those met with in the former type.

Pyrexia of an undulatory character, unaccompanied by suppuration, is the one constant feature of this disease. The initial symptoms are tightness about the throat, often redness of the tonsils, and slight swelling of the submaxillary and cervical glands, pain in the muscles of the neck and back, nausea, anorexia, epigastric tenderness, headache and foul tongue. The usual signs of fever supervene with especially marked dyspeptic symptoms and constipation. Remissions of temperature are accompanied by most profuse perspiration. The reflexes are increased; and at any stage, but usually later in the attack or during convalescence, acute sciatica or other localised neuritis may occur in any position. Or there may be acute effusion into one or more joints, or acute orchitis. Finally, long cases may be reduced to an anæmic, emaciated and bed-ridden condition, the patient being subject to attacks of bronchial catarrh, cardiac palpitation or neuralgic complications on the slightest chill, change of weather or even excitement. Disappointed at each relapse and his hair fallen off, his whole expression becomes the picture of despondent apathy, his only wish being to get away to England. His emaciated appearance, profuse night sweats with intermittent pyrexia and cough, remind one forcibly of phthisis, a diagnosis which is often erroneously made. However, in time the tongue shows signs of cleaning, the temperature falls to subnormal and the corner is turned, after which, under judicious dietary and plenty of fresh air, he regains weight and strength with wonderful rapidity.

Prognosis.—Favourable as regards danger to life or health, the case mortality being only about two per cent, but most unfavourable as regards the length of attack and consequent interference with livelihood until convalescence is complete. The pyrexial duration (20 to 300 or more days) averages 60 to 70 days. Previous history of tuberculous, cardiac or pulmonary disease, is unfavourable; while the actual presence of cardiac or renal disease, of concurrent anæmia, of phthisis or of great nervous excitability, indicates a serious prognosis. The only reliable sign of approaching convalescence is a subnormal temperature for a few days, followed by a normal, steady temperature when accompanied by a clean or rapidly-cleaning tongue.

Second attacks are rare. It is not certain to what extent one attack protects against another, but it seems that it confers some immunity.

Morbid anatomy.—The naked eye post-mortem appearances of acute and rapidly fatal cases are those of intense congestion, especially marked in the internal organs, the spleen being enlarged, often disorganised, and almost liquefied within its capsule. In chronic cases there are the signs of long-continued irritation of the tissues, similar to the fibrotic changes consequent upon chronic alcoholism or plumbism.

Diagnosis.—The disease can be definitely diagnosed from enteric fever, paludism, phthisis, liver or pelvic abscess, empyema and other suppurating diseases, rheumatic affections and croupous pneumonia, etc., by the reaction of the blood serum of true cases, upon living or dead cultures of the micrococcus melitensis;[1] also by the local and special symptoms of these diseases, and the absence from the blood of malarial parasites. The serum reaction is often the only reliable sign, so closely does the disease resemble enteric fever as met with abroad.

Prophylaxis.—The institution of sound water drainage, the avoidance of contaminated ground for camping purposes, the prevention of pollution of the soil round camps and buildings, due attention to all latrines and urinals, proper ventilation, avoidance of damp and overcrowding, and destruction of infected stools and urine are the most effectual means of prevention. It is also desirable to avoid Mediterranean towns between the months of May and October, and to remember that this region is, except in

[1] For technique, see *Mediterranean, Malta or Undulant Fever* (author), p. 158; Macmillan and Co. 1898; and Wright in *Brit. Med. Journal*, 1897, vol. i. pp. 139, 258.

the hot summer months, subject to sudden changes of temperature and that the air is very moist, necessitating the possession of the warmest clothes, an extra cloak at sundown, and of always sleeping in flannel, and wearing it next the skin.

Treatment.—No agent having a specific action upon this virus is known at present. We have primarily to treat a pyrexia, and secondly such local symptoms as may be present. First remove the patient to sanitary surroundings; when the diagnosis is certain open the bowels with a smart purgative, calomel with compound jalap powder for choice. Confine the patient to bed so long as the high temperature continues. Let him have as much fresh air as is compatible with avoidance of chills and the fatigue of moving, placing him, when possible, in his bed, at least during the daytime, out in the open air on a verandah or elsewhere. Provide an ample supply of night clothes of some absorbent material for the changes necessitated by the excessive diaphoresis. Keep the temperature at or below 103° F. by means of tepid or cold sponging or packing. Treat any tendency to pneumonic congestion or weak cardiac action at once and energetically. Attend to the skin, washing it daily with tepid water containing a little ammonia or vinegar. Diet to be fluid so long as fever is present, restricted in amount when that is high and abundant when low. Chronic cases, with mild intermittent temperature, can often digest and benefit by scrambled eggs, or fish, etc., for breakfast when the temperature is normal, but not later in the day when it rises. The tongue is the best guide as to the suitability or otherwise of dietary. In the early morning, about 5 or 6 A.M., a glass of milk should be given (with or without whisky) as a routine practice, the patient being extremely depressed at that time. Subnitrate of bismuth should be given for gastritis or vomiting, combined if necessary with beef juice, peptonised foods and champagne. If diarrhœa is present, beef tea is contra-indicated. For diarrhœa resulting from irritation in the colon, warm enemata of starch and opium are useful. Fresh fruit and lemonade should be given, stewed prunes and baked apples being utilised to lessen constipation. Effusion into joints and neuralgic pains are best treated by moist warm local applications, followed by belladonna and by placing the patient between blankets and enveloping the part in cotton wool and flannel. Though the bed pan is necessary during acute pyrexia, the close stool may be used in the chronic intermittent stages, provided the patient's hips, etc., are carefully protected from cold. Quinine and arsenic do harm in the acute stages; but during convalescence quinine may be given in small doses as a tonic, or better still

Blaud's pills, with plenty of out-door air, full diet and stout, but fatigue and mental worry must be avoided.

During the autumn and winter months cases do better away from England and where they can be out of doors, in hill towns of Italy or Sicily, or in the dry climate of Egypt. During spring and summer a change to England, Switzerland, the Italian Alps or similar places is most important after the first acute stage has passed. A dry place is essential, bracing but not exposed. A sea voyage is often most beneficial to long chronic cases, especially when the patients are able to get on deck.

Other treatment should be on general lines, such as is usual in enteric fever, for the acute stages, and that now recommended for phthisis during the chronic stages.

M. Louis Hughes.

CHOLERA

An acute infectious disease, determined by a specific organism termed the "comma" bacillus, which is met with on and between the epithelial cells of the intestinal mucosa and in the contents of the bowels, and characterised by intestinal evacuations of a watery consistence, by violent vomiting, by muscular cramps, by suppression of urine, by extreme and rapid prostration, and by a high mortality. Endemic in Lower Bengal, and perhaps in other parts of Asia, cholera frequently assumes an epidemic character, spreading to almost every part of the world.

History.—Although cholera was well known in Asia and Europe from early times, the disease was first definitely described during the epidemic of 1817 by Europeans in India. In 1830 the disease visited Europe for the first time during the present century, and since then it has reappeared in the following years: 1845, 1853, 1863, 1873, 1884, 1892, on each occasion lasting for one, two or three or more years before it finally disappeared. The first three epidemics only were general, every nation in Europe being severely visited by cholera, but since 1865 the outbreaks have been very limited, a few towns only in several countries being the sole sufferers.

Geographical distribution.—Cholera is an Asiatic disease, and belongs more particularly to certain areas in Lower Bengal, so much so that in this region cholera is held to be endemic. The

attempts to focus the origin of all cholera epidemics in Bengal is probably based on ignorance, as cholera is prevalent in many other Asiatic countries at some period of almost every year. Geological conditions play, if any, but a secondary part in determining the presence of cholera; elevation *per se* has less influence than used to be assigned to it. It is a disease that travels along the lines of human traffic be they by road or rail, by steamships or river boats. Cholera has visited both hemispheres and spread almost universally, yet there are some regions even in India, such as Mooltan and Pondicherry, where immunity is more or less complete. Australia, New Zealand, the Cape of Good Hope, the Andaman Islands in the Bay of Bengal, and the majority of the islands of the Pacific have never been visited by cholera in an epidemic form.

Etiology.—*Predisposing causes:* season, exercises, a direct influence on the presence of cholera in all countries to the north of the Equator. July and August are the months during which it attains its maximum of virulence; but it may, and does occur during the winter months in India and in Russia, where it has continued throughout the snow and Arctic cold of the severest winters. Insanitary localities are, as a rule, subject to be severely visited by cholera; whether the insanitary state be due to overcrowding, foul drains, water-logged soil, absence of drains, polluted water supply, leaking cesspits, or to all combined, each is warranted when cholera is imminent to increase the death-rate in direct ratio to the amount of insanitation. A new arrival is more liable to be attacked than the native or old-time European resident when cholera is prevalent. Women are less liable to cholera than men, and infants enjoy a marked immunity. Alcoholic intemperance, bad or insufficient food, fatigue from whatever cause, fear of infection, debility brought about by illness from any cause, be it climatic, malarial or "constitutional," predisposes the individual to attacks of cholera when it is epidemic. Europeans are most liable to a seizure of cholera during the night, and natives after a full meal. In the tropics the former, intolerant of the heat at night, unconsciously, it may be, throws off his bed clothing and renders himself more liable to abdominal chill at a period when his own temperature is at its lowest and the temperature of the air is at its minimum. The native is seldom so affected, and it has been repeatedly observed that a full meal, especially of fish or oysters, serves as a predisposing cause.

An attack of cholera affords protection for a time only. A

second attack during any single epidemic is well-nigh unknown, but a previous attack confers no immunity from cholera during future outbreaks.

The means by which *the poison is introduced into the body* is at the present day held to be by pollution of the drinking water by cholera evacuations. In 1854, Dr. Snow, by his careful investigations, established the power of water contaminated by cholera evacuations to cause cholera, and many instances could be cited in proof of the principle which he first enunciated.

It is possible also that food, merchandise, insects such as flies, clothing, etc., may serve as a medium whereby cholera can be communicated, but although these may serve to infect individuals, they cannot serve as a general infecting agency, unless the stools of one or more of those so suffering reach the drinking water used by the community.

Bacteriology.—The introduction of the specific toxin into the body is the one exciting cause of cholera. Koch, during the Egyptian epidemic in 1883, separated a bacillus from the stools and intestines of persons suffering from Asiatic cholera. This microorganism is known from its shape as the "comma" bacillus, and its presence in the stools in quantity is a conclusive proof that the person is suffering from Asiatic cholera.

Methods of microscopic examination.—(*a*) Smear a small quantity of, or a mucous film from, a cholera evacuation on a warm slide; allow this to partially dry; drop a few drops of a weak, freshly prepared, watery solution of methyl violet on the specimen, and after fifteen seconds run the staining fluid off; superimpose a cover-glass, pressing it down lightly; lay a piece of filter paper on the cover-glass and slide, so that the superfluous fluid at the cover edge is absorbed; examine with a one-tenth or one-twelfth inch oil immersion lens. By this procedure the bacilli are stained, their vitality and power of movement are not checked, more especially if the slide be maintained at a temperature slightly above that of the body.

(*b*) Place a small quantity of the cholera evacuation on a cover-glass; superimpose another clear cover-glass and pull the two asunder; dry the specimen in the usual way; float the cover-glasses, smeared side downwards, on a watery solution of fuchsin in a porcelain dish, and warm over a spirit-lamp flame for ten minutes. Dry the preparation and mount it for microscopic examination.

(*c*) For more precise investigation the bacillus may be stained by Löffler's method, which, though a tedious process, gives more precise results, and by it the flagella are best defined.

The comma bacillus, cholera vibrio, or spirillum choleræ Asiaticæ, present in the stools and in the intestines of cholera patients, but never found in the blood or tissues, has the following microscopic characters:—

The typical bacillus measures 1 to 2 μ in length and 0.5 to 0.6 μ in thickness. When stained the parasite shows one, two, or three, more deeply coloured spots, suggesting spores, although sporulation has never been observed. The bacilli, which are usually seen to be separate, may coalesce so as to form an arc; but when the commæ are joined with their curves in a reverse direction the body appears curved like an "S." In some preparations from cultures the bacilli may coalesce by their extremities, so as to form an undulating thread-like line (Plate II.).

When stained the comma bacillus exhibits, during certain as yet undetermined periods of its existence, extremely fine flagella. In some specimens but one is met with, although a flagellum at each end would seem to be the rule. The flagella may exceed in length the body of the bacterium, and, although very delicate, confer upon the organism active "spirillum-like" movements.

But the comma bacillus is not the definite entity one anticipates from reading Koch's original description. In the first place, there are several bacilli which bacteriologically and anatomically resemble the comma bacillus of Koch. Of these the best known are the bacilli of *cholera nostras*, certain bacilli met with in the mouth, and even in so-called "fresh" water. Nor do the comma bacilli of cholera always maintain the power of infection claimed for them. Cultures of the comma bacilli from cholera stools have been swallowed by several experimenters with negative results. Again, the bacilli have not always been met with in the stools of cholera patients, and moreover bacilli, comma in shape and bearing seemingly specific characteristics, have been frequently met with in the stools of healthy persons. An accumulation of observations of a like nature have thrown doubt upon Koch's dogma that the comma bacillus is the only essential element required to produce an attack of cholera. Still, for clinical purposes the presence of the comma bacillus in quantity in the stools justifies the conclusion that a specific disease—Asiatic cholera—is present.

Culture, methods and characters.—The cholera bacillus yields a well-nigh specific appearance in culture media. It will not grow on sour or acid media but thrives luxuriantly on broth, milk, or serum that has been rendered alkaline. Agar-agar is not liquefied during the process, but gelatine is so readily, and it is for purposes of diagnosis

the most suitable culture medium. When gelatine is seeded by punctures and maintained at a temperature of 20° C., within twenty-four hours a delicate white cloud forms along the puncture tracts. The gelatine liquefies, and in forty-eight hours the liquefied areas assume a characteristic funnel shape at the upper part. By the fourth day a pronounced thread-like process extends downwards into the medium. The thread is spiral and presents enlargements in its length like the links of a cable. The whole of the upper or seeded portion of the gelatine liquefies, and the contents of the tube present the following appearance:— Lying on the top is a grayish scum consisting of involuted or degenerate forms of the comma bacillus; beneath the scum is the clear liquefied gelatine; and below this, and resting on the solid gelatine, is a yellowish-white layer of cholera bacilli. When gelatine plate-cultures are employed, the various colonies are seen to be irregular in shape and size, and to give a granular, shining, ground-glass-like appearance to the gelatine medium. A faint roseate tinge is imparted to the growth in the later stages, a colour considered to be characteristic of cholera bacilli. When grown on sections of sterilised potatoes, at a temperature of between 30° C. and 35° C., the exposed surface of the potato is speedily covered by a copious moist-looking growth of a dirty gray or light brown colour, altering to colours of varying tints in the course of a few days.

Incubation.—After exposure to cholera, infectious symptoms may develop in a few hours. Three days is the usual period of incubation, but it may extend to as many as ten days. This question has a direct bearing on *quarantine*, in fact all quarantine regulations against cholera are founded on the determination of this period. Should a ship be ten days out from a cholera-infected port, and no cases of cholera have occurred on board during the voyage, it is foolish to impose a further period of quarantine upon the passengers.

Symptoms.—It is customary to divide an attack of cholera into four stages, viz.: (1) the Premonitory stage; (2) the Evacuation stage; (3) the period of Collapse or Algide stage; and (4) the stage of Reaction. These are more or less fanciful divisions, as in a large number of cases the onset is sudden, the development explosive, and death a matter of a few hours.

The *premonitory diarrhœa* of cholera is a condition more often described than seen, and how far it is an essential stage of the disease or an accidental predisposing condition is doubtful.

The *onset* of cholera is marked by a violent intestinal flux, attended by a feeling of sinking in the epigastrium and a marked loss of strength.

The stools in cholera are characterised by their consistence, bulk, frequency, and the force with which they are expelled. At first they consist of copious watery evacuations bearing a resemblance to fæces, but they speedily lose every trace of fæcal matter and become the typical "rice-water" stools characteristic of the disease. These evacuations, on being allowed to stand, separate into a sediment and a whey-like fluid. The former consists of active amœboid cells, epithelium, hyaline, and granular cells, the bacteria which usually inhabit the intestine and the specific comma bacillus. The fluid has a specific gravity of 1005 to 1010, and gives a neutral or faintly alkaline reaction, and contains a little albumen. The bulk of the motion is at times surprising; well-nigh a quart may be passed at a time. The frequency of the calls to defecate allows of but little time to remove one bed pan before another is wanted. Owing to the violent contractions of the muscular walls of the intestine the contents of the bowel are expelled with great force, leaving the patient prostrate for a few minutes, or until the next motion threatens.

Copious vomiting without great effort sets in, the vomited matters being first the stomach contents, but afterwards consisting of thin fluid containing a little mucus. Cramps in the limbs and muscles of the abdomen give rise to considerable pain, the patient crying out in dread when a muscular spasm comes on. Thirst is present almost from the first, but the patient vomits whatever he drinks to relieve it. After a few hours the strength of the patient reaches a low ebb. The tongue looks sodden, the gums pale; the surface of the body feels cold, and if the temperature is taken in the axilla it will be found lowered; it may be two, three, or four degrees below the normal. The pulse, which is accelerated from the onset, soon becomes feeble, then thready, and in very serious cases cannot be felt at the wrist or even in the arm. The heart sounds, when the disease is well advanced, are scarcely to be heard, and the cardiac impulse disappears. The breathing is disturbed, becoming gasping, the patient calling out for air; the voice is reduced to a whisper; the expired air is cold; there is much restlessness, tossing about, and throwing off the bed-clothes. The urine, which is at first high coloured, soon becomes scanty and albuminous, and may be altogether suppressed. Should this state continue, a grave condition is indicated.

When the *stage of collapse* supervenes the evacuations may cease, though the vomiting may continue, and the cramps give rise to no expression of pain. The skin appears cyanosed and wrinkled, and when seized between the finger and thumb the fold disappears

quite slowly. The face looks shrivelled and lined, the eyeballs sunken, the eyelids are but half closed, and the nose looks pinched and pointed, the features being so changed as to render the individual well-nigh unrecognisable. The mental condition, which in the early stage is quite clear, in the later stages changes to one of apathy. Whilst the thermometer in the mouth and axilla registers 4° F. to 6° F. below the normal, the rectal temperature rises usually to 103° F. or 105° F. In several instances, in the experience of the writer in Egypt and China, the rectal temperature reached to between 108° F. and 109° F. half an hour before death.

Should death be delayed beyond the stage of collapse, what is termed the "tepid" stage supervenes. The body temperature rises to about the normal: even the pulse may return at the wrist; the purging and vomiting entirely cease and the patient's features and complexion become more natural; but the pupils remain fixed, the cornea hazy, the eyeballs sunken, and in a comatose state life becomes extinct. There are practically no recoveries from this stage, although to the inexperienced it would seem that a favourable turn has set in.

When the attack is followed by *reaction*, the surface of the body becomes warmer, the colour begins to return, the pulse and voice recover, urine is passed, and after a sleep the patient wakes refreshed. On the other hand, when the stools are passed involuntarily, when the brachial pulse or even the carotid pulse disappears, when hiccough becomes distressing, and the temperature falls to, say, 94°, whilst the temperature of the rectum rises perhaps to 105° or 107° F., a fatal issue is at hand.

Sequelæ. — Convalescence, following an attack of cholera, depends upon the duration and acuteness of the attack. In mild cases convalescence is rapid, but in severe and prolonged cases the intestines may remain irritable for months. Many ailments and conditions may succeed an attack of cholera, such as an urticaria or *roseola choleraica*, convulsions, especially in children, enteritis, hæmorrhage from the bowel, parotitis, anæmia, insomnia, albuminuria, sloughing of the cornea and scrotum, and pulmonary thrombosis. Females frequently abort during, or very soon after an attack.

Diagnosis.—Diarrhœa from any cause, which is attended by lividity of complexion, mental anxiety and epigastric sinking, is apt to be styled "choleraic." Any septic or poisonous material taken as food may set up symptoms simulating Asiatic cholera; but it is only by bacteriological cultivation and by microscopic

examination of the intestinal dejecta that the actual existence of true (Asiatic) cholera can be conclusively diagnosed.

Prognosis.—Persons attacked by cholera at the commencement of an epidemic are in greater danger than those seized when the epidemic is on the wane. Children, persons in advanced years, chronic sufferers from any form of visceral disease, are less able to withstand the onset of cholera than are young and middle-aged persons in good health. Yet the strongest men may succumb speedily. The writer knew of an engine-driver, in Egypt in 1883, who started on his engine at Alexandria in perfect health, die before he reached Kaffir-Zayat, halfway to Cairo, the journey lasting only two and a half hours.

Mortality.—The death-rate of different epidemics varies, and the case mortality at the commencement and end of an outbreak shows different degrees of virulence. It may be taken as a rule that half the persons attacked by cholera die, the proportion during the earlier part of the epidemic being about 65 per cent of those attacked, and during the later stages 35 per cent.

Post-mortem appearances.—As may be gathered from the symptoms, the body generally will present a shrunken appearance after death. The rectal temperature usually rises for the first half hour; rigor mortis sets in very early—within an hour or two, and muscular contractions may distort the limbs and cause them to change their position. The stomach is usually empty, though a considerable quantity of food may remain in it in spite of incessant and copious watery vomiting. The intestines contain some fluid matter with mucous material intermixed. The mucous surface of the alimentary canal looks sodden, bleached in parts, and congested in others, and the mucous and submucous coats may be easily peeled from the intestinal walls. The solitary and agminate glands are swollen. The gall bladder is distended with bile, the liver and kidneys appear duskily congested and full of blood, and the spleen of the same colour may be either enlarged or diminished in size. The large veins of the trunk, the right side of the heart, and the pulmonary arteries are usually distended with blood, whilst the limb veins are empty. The lungs are pale, and seem as if contracted and drawn in towards their roots; the muscles of the limbs and trunk, when cut into, present at times a dark, violet-tinged appearance, but in other cases they look pale and bleached. It is not uncommon to find muscles ruptured, the result of the severe cramps and spasms during life. Should the patient not have succumbed until the period of reaction

has set in, symptoms of congestion in the lungs, and of the intestines, or even inflammation of these organs, may be met with.

Treatment.—*Prophylactic* treatment during a threatened epidemic of cholera resolves itself into the individual efforts of householders to procure boiled water for drinking, for washing utensils, and for baths. Milk should be scalded or boiled before being consumed, and locally manufactured ærated waters should be eschewed. The further care to be taken is strict attention to diet, which should be as simple as possible, and well cooked. Unripe and rotting fruit should be forbidden, but fruit in season and in good condition should be allowed. The writer, by removing the restrictions against the consumption of fruit in good condition, in the towns under his care in Egypt in 1883, found immediate benefit therefrom. To the poor in Egypt and most Oriental countries fruit is a stable means of subsistence, and by withholding it entirely the native is more or less reduced to well-nigh starvation point; and inanition is the handmaiden of cholera.

Above all is it imperative to disinfect the dejecta of cholera patients; and not only should the stools be dealt with, but even the vomited matters, the soiled clothing and bedding. The utensils into which the patient evacuates should contain a potent disinfectant such as perchloride of mercury (1-2000), or carbolic acid (1-20). The evacuations must be covered completely by the disinfecting fluid, removed from the sick-room, and, where possible, buried at least three feet deep in the ground in a place remote from possibility of contaminating wells. On no account must the evacuations be thrown on the surface of the ground near the house, into open drains, cesspools or middens. Where a water carriage system is effective they may be consigned to the sewer, which ought to be frequently flushed by a disinfectant; the ferrous sulphate (1 oz. to 1 pint) is eminently satisfactory for the purpose. Clothing and bedding are to be burnt; and should the patient die the body ought to be cremated, or, when that is inexpedient, the remains should be coffined in charcoal, buried at least six feet in the ground and covered by lime before the earth is replaced.

Treatment by anti-choleraic inoculations.—As a preventive measure in cholera, inoculations by a specially prepared virus have been systematised and practised by Haffkine in India. By his method protection against cholera is afforded by "acclimatising" the system, first to a weak, and afterwards to a strong cholera poison. A pure culture of the weak or attenuated virus is grown in a medium (agar), at a temperature of 39° C.; a constant æration being

maintained during the process. The strong or "exalted" pure culture is grown in the peritoneal cavities of a series of guinea-pigs. As each animal dies the fluid in the peritoneal cavity is removed and transferred to another, and so on through a series of twenty or thirty guinea-pigs, until a maximum toxicity is obtained. From the pure cultures the respective "weak" (first) and "exalted" (second) vaccines are prepared by cultivation on agar and conversion into emulsions by superimposing a layer of broth with which the growth is intimately mixed. In this form the respective "vaccines" may be used,—"living vaccines"; or they may be treated before being injected by the addition of dilute carbolic acid, "carbolised vaccine," by which process the bacilli are killed. In the one case the bacilli and their toxins are injected together, and in the other the toxins, deprived of their bacilli, are employed. As in the "living vaccines" the bacilli die immediately after the fluid is injected subcutaneously, the choice of either form seems immaterial.

Under strict precautions to ensure sterility during the operation the attenuated vaccine is injected under the skin of one flank, and on the fourth or fifth day afterwards the stronger vaccine is injected into the opposite flank. The quantity used is one cubic centimetre for an injection.

The signs and symptoms produced by inoculation with Haffkine's serum appears some three hours after the hypodermic injection has been given. Tenderness is experienced at the seat of the puncture and a slight œdema extends for some little distance around; a febrile disturbance and consequent headache, loss of appetite, and general feeling of lassitude is set up, which, however, pass off within forty-eight hours, and by the fourth day all the signs at the seat of injection disappear. A similar train of symptoms is set up after the second inoculation, but the febrile disturbance, although of shorter duration, is more acute.

Repeated and careful experiments in animals convinced Haffkine of the efficacy and safety of the remedy, and, seeing that up to the present moment well-nigh 100,000 persons have been inoculated without any untoward result, the safety of the remedy may be regarded as proved. Haffkine published the results of his inoculations in a paper read before the Royal Society (June 1899). He states that some 8000 persons were inoculated with the prophylactic serum in Calcutta, and for two years observations were made as to the relative advantages derived therefrom. The majority of the inoculated resided in the same neighbourhood, and in many instances in the same house with members of the family

who had not been inoculated. Whilst the uninoculated developed cholera in a marked manner, the inoculated showed practically complete protection until the 420th day, when cholera began to spread amongst them. Moreover, Haffkine showed that it was only as a temporary prophylactic that the inoculation served, for the proportion of deaths to cases amongst the inoculated and the uninoculated remained the same. The efficacy of the remedy against cholera is still on its trial, but there is every indication that a prophylactic remedy of great value has been discovered.

Medicinal treatment.—When diarrhœa occurs whilst a cholera epidemic is incident means should be taken to check it. For such purposes many drugs are recommended; some authorities claiming, quite unjustifiably, well-nigh specific action for their plan of treatment. The writer can speak from experience, approvingly, of Macnamara's pill of 1 grain of opium and 4 grains acetate of lead given early in the disease. Chlorodyne in 30 drop doses has many, perhaps most advocates; others recommend 5 to 10 grains tannic acid, whilst some prescribe 20 minims of spirit of camphor, or 10 grains of Dover powder, or 20 minims laudanum with 3 grains of Cayenne pepper; the drug being repeated at short intervals as symptoms necessitate. There is no doubt that diarrhœa can be arrested by one or other of these remedies during a cholera epidemic, as at other times, but whether the flux of true cholera can thus be checked is doubtful.

When cholera has reached the second or evacuation stage no medicinal or other forms of treatment, if we exclude anti-choleraic inoculations, possess a specific action. The medicinal treatment of cholera is purely empiric, and one has to fall back on the time-worn expedient of treating symptoms as they arise.

Attempts to stem the intestinal flux by astringents are, at this stage of the disease, useless; their powers are rendered abortive by the rapidity with which they are hurried along the canal. In fact, purgatives have more advocates than astringents at this phase of cholera. Dr. George Johnson endeavoured to place the purgative plan of treatment on a scientific basis, and administered moderate doses of castor oil frequently repeated. The rationale of this treatment is that the cholera poison is thereby eliminated from the intestines and nature is aided in her attempts at so doing. Reasonable as this treatment might seem to be, experience has declared against it. There is the danger of the purgative continuing the purgation at a period of possibly natural abatement of the disease, when rest and quiet to the intestines and the body is of vital consequence. Rest in bed, warmth with free circulation of warm

air is essential. The patient should not be allowed to get up to stool, nor sit up in bed to drink. Ice to suck, or, in its absence, hot (not cold) water to drink should be freely supplied, and will help to allay thirst and vomiting. A mustard plaster to the pit of the stomach and hypodermic injections of morphia with atropine will tend to allay vomiting and relieve epigastric pain and restlessness. Cramps are to be relieved by firm rubbing by the hands, and cardiac weakness by hypodermic injections of ether or digitalin. Placing the patient in a recumbent position in a warm bath 103° F. is an excellent form of treatment; and may be supplemented by injecting ice-cold water into the rectum whilst the patient is immersed in the hot water. Slow intravenous injection of a saline fluid consisting of 60 grains of common salt and an equal quantity of carbonate of soda, dissolved in a quart of boiled water at a temperature of 100°, 103°, or even 105° F. has been administered with advantage. Of other methods the wet sheet, spinal ice-bags, intraperitoneal injections of warm water and hot-air baths, have perhaps most to recommend them.

Suppression of urine must be treated by dry cupping over the kidneys, or by poultices or hot fomentations round the waist; intestinal irritability may be counteracted by bismuth and opium, and by the wet pack to the abdomen.

All food should be withheld during the stage of vomiting and purging, and, should the stage of collapse supervene, food given by the mouth can do nothing but harm. Stimulants, champagne especially, are indicated.

When the stage of reaction sets in, hastiness in administering "nourishing" foods is to be condemned. Milk-whey, white-wine whey or koumiss should be given in teaspoonful doses at frequent intervals, every few minutes in fact. Freshly-made tea, with or without a small quantity of whisky or brandy, sipped slowly and either warm or iced, is grateful to the patient. Rice tea (boiling water poured over rice roasted brown) is a pleasant and nourishing drink with or without lemon. Soon more substantial food is wanted. Starchy foods are to be avoided and a meat diet commenced at first. Raw meat juice, scraped beef, plain jellies, etc., are to be given in small, even minute quantities, and frequently repeated. In a day or two, finely-minced beef hastily and very lightly cooked may be relished. Of starchy foods, well-boiled rice is the first to be given, and then bread which has been well baked.

JAMES CANTLIE.

PLAGUE

The term plague was employed in ancient, and up to quite modern times to signify the prevalence of any epidemic disease attended by a high rate of mortality. The word is now, however, no longer used in a general sense, but as the name of a definite disease bearing specific characters. There is in consequence considerable confusion in determining the accurate history of the actual disease, as many ancient and mediæval writers employed it indiscriminately. The "black death" which devastated Europe in the fourteenth century, and the "great plague" which raged in London in 1665, were without doubt plague as it is now understood.

Plague is a specific, acute, contagious disease, appearing in epidemic form, attended by a high mortality and with a tendency to linger and recur once it has attacked a community. It is characterised by a febrile state, by the development of buboes in the deep and superficial glands, and by changes in the lungs, spleen, and other organs. A specific diplococcus is met with in the blood, excretions and viscera of persons suffering from, or who have died of plague.

Geographical Distribution.—During the latter half of the nineteenth century plague has been met with in Europe, Asia, and Africa. In 1853, and again in 1873 and 1897, plague existed in Western Arabia; in 1858 and in 1874 it appeared in Tripoli; the northern part of Persia was severely visited in 1863, and again in 1870. Mesopotamia from 1874-1877 proved the centre of a widespread epidemic which reached northwards to the Caspian shores, advanced up the Volga in 1878, and extended westwards as far as Syria and eastward to Persia.

Since plague appeared in South-Eastern China in 1894, it has been met with in Formosa, Annam, and the Bombay Presidency as a severe epidemic; in Southern India, Calcutta, on the shores of the Persian Gulf, at the port of Mecca, in the islands of Mauritius, Réunion, Madagascar, and Penang, and in the towns of Alexandria and Oporto it existed in a mild form during 1898-1899. Koch has demonstrated the presence of plague in the districts of Bukoba and Kitengule in German East Africa; and from the hinterland of the French possessions in West Africa plague was reported during

1899. The malady first reached the American continent in 1899, appearing at Santos, a seaport town of Brazil.

The disease has been long known as *Máhámarí* in the districts of Kumaon and Ghurwal in the north-west provinces of India; and in the Chinese provinces of Sze-chuen and Yunnan on the borders of Thibet many writers have described it under the name of "Yunnan" plague. Hence Kumaon and Ghurwal in India, and Sze-chuen and Yunnan in China, are held by many to be the endemic seats of plague.

Etiology.—Plague is held to be one of the "filth" diseases, and it attacks principally the least sanitary parts of every city. In proportion to the extent of insanitation, so does the severity of the outbreak vary. Infants and aged persons are less likely to contract plague than are the others of the community, but sex seems to be no protection. Plague prevails as a rule during the cool weather in tropical countries, great heat causing a subsidence in its virulence. In contradistinction to this general rule there are several exceptions, for in Hong-Kong and Poona in 1899 plague was at its maximum during the hottest part of the summer. Europeans dwelling in close proximity to plague-stricken areas in Asia, suffer or escape in proportion as they live after the manner of the natives, or in the more sanitary state of Western Europe.

Bacteriology.—In 1894, during the epidemic of plague in Hong-Kong, Professor Kitasato of Japan discovered the plague microbe, and since then the presence of the organism has been noted in the blood, secretions, and organs of persons suffering from plague wherever the disease has prevailed. Experimental investigations show that the disease can be communicated to several of the lower animals, and all observation goes to show that the bacterium known as the plague bacillus (Kitasato) is the cause of the disease.

Simultaneously with, if not antecedent to, an outbreak of plague rats are attacked by all the symptoms of plague, and die in great numbers. Other animals may also be attacked, but none are so prominently or so constantly affected.

The bacillus of plague has been found in the dust and filth of infected houses, but the exact relation of the disease to the soil, if indeed the soil bears any part in the life-history of the parasite, has not been ascertained. Certain it is, however, that the bacillus thrives better in some localities than in others, where there is but little difference in latitude or sanitation. This is well instanced in the cases of Bombay and Calcutta. In the former, plague at once

became severely epidemic, whilst in Calcutta the disease for several years appeared in a mild, almost a sporadic form.

The microbe of plague is met with in the fluids which surround an inflamed gland, in the gland itself, and in the pus from a newly-opened bubo. The bacillus is also found in the spleen, lungs, liver, kidneys, stomach, and intestinal walls. In the saliva, the expectoration, the fæces, and the urine the micro-organism has been shown to exist. In the blood the bacillus is easily demonstrated in the later stages of fatal cases, but frequently it is only to be found in infinitesimal numbers in the earlier stages of the disease.

The plague bacillus is readily stained by all basic aniline dyes, when it is to be seen as a short flagellated rod with rounded ends measuring 1 μ in length and 0.3 μ in breadth (Plate I.). At each end the bacillus stains more deeply than in the centre, and sometimes a clear area round the bacillus can be seen. In stained cover-glass preparations the bacillus resembles a diplococcus, but occasionally four to six of the bacilli in culture preparations are seen to form a chain simulating streptococci. The microbe does not sporulate; in fresh specimens it is seen to be motile. The best culture medium is one composed of "a 2 per cent alkaline solution of peptone containing 1 per cent gelatine" (Wilm). A temperature between 36° C. and 39° C. is the most favourable for the growth of the bacillus. At a temperature below 25° C. and above 40° C. a decline in the rapidity of the growth becomes apparent. "On gelatine plates the bacillus grows without liquefying the medium, and produces in forty-eight hours small, round, grayish-white colonies" (Wilm). On bouillon the growth of the bacillus forms at the bottom and along the sides of the test-tube as a granular or flocculent precipitate, whilst the bouillon itself remains clear. When the tube is shaken the precipitate is distributed through the fluid. On potato, at blood-heat, a very delicate, scanty, grayish-white or white crusted growth is formed after thirty-six hours. On agar plates two forms of colonies are met with, a large and small, and, when puncture cultivations in agar tubes are made, the seed from the smaller colonies shows a scantier growth than that from the larger. This variability of the plague organism in regard to growth is borne out experimentally in regard to its toxic power.

Communicability.—Plague can be carried by persons or animals suffering from plague, and by articles of clothing, food, or water which have become contaminated. Although the disease is to some extent transmissible, it appears that, with ordinary care, there is no great danger of contracting it. It is seldom that either doctors, nurses, or sick attendants are attacked through attendance at plague hospitals, provided precautions are taken, such as

sleeping in good quarters, taking meals away from the hospital, etc., etc. The disease is, however, certainly contagious and inoculable. A nursing sister in Hong-Kong who had been through two epidemics of plague succumbed to the disease brought on by receiving the expectoration of a delirious patient on her conjunctiva. Two of the Japanese physicians, studying plague in Hong-Kong in 1894, were inoculated at a post-mortem examination, and suffered severely. Animals, such as cattle, pigs, dogs, and especially rats and mice, contract plague, and, possibly by their contaminating human food, become a source of infection. This fact accounts, no doubt, for the belief that grain is a source of infection. Food may also be rendered infectious by flies. The clothes of persons suffering from plague harbour the virus, as shown by Wilm, who succeeded in cultivating the bacillus from portions of clothing that had been soiled by the urine or fæces of plague patients. The water of various wells was found to contain the plague bacillus in Hong-Kong during 1896. The plague bacillus may enter the body by the skin. This belief was surmised owing to the frequency with which the bare-footed coolies in China showed groin buboes. There is reason to believe that flies and fleas may communicate the disease. It is presumed that the virus can be inhaled, owing to the frequency with which primary pneumonia appears during some outbreaks. The bacillus may also enter the body by the alimentary canal. This is known to be the case as the result of feeding animals with cultures or infected food.

Incubation.—From three to five days is the usual period of incubation. Statements that incubation may vary from a few hours to eight days, or even longer, are probably to be explained by the source of infection having been mistaken.

Symptoms.—*Prodromal symptoms* are seldom observed, but for a day or so before the disease sets in, lassitude, loss of appetite, and pain in the loins have been recorded.

Invasion.—The symptoms of plague are generally ushered in suddenly by a rigor accompanied by a hot and dry skin, headache, and marked prostration. The face is dusky, the eyes sunken, the features drawn, and the expression vacant. Mental ineptitude is shown from almost the first onset of the disease. *Fever* is a constant symptom in all cases of plague. In a certain proportion the temperature runs up in an hour or two to 104° F. or higher, but the maximum is usually attained on the third or fourth day, when the thermometer registers frequently 106° F. or over. Very high temperatures are not, however, by any means constant; the thermo-

meter may never register over 101° F. After a sudden initial rise the temperature in a day or two may fall below normal; on the other hand, it may remain high till death occurs, or in cases of recovery fever may continue for weeks. Curiously enough the presence or absence of high fever gives no guide to the chance of recovery, as many patients in whom the temperature fell to the normal after a day or two succumbed, or, on the other hand, recovered as readily as those in whom the fever continued high.

Variations in Type.—Several terms are employed to denote varieties in the signs and symptoms of plague: bubonic, intestinal, pneumonic, convulsive, toxic, typhus type, pestis siderans, pestis ambulans, pestis minor. These terms, for the most part, explain themselves. The viscus indicated may alone show signs and symptoms of being affected. A toxic form implies that the symptoms resemble a septicæmia, no local signs developing. Siderans indicates a rapidly fatal form, and ambulans a mild type, during which the patient may not even be confined to bed. The last mentioned however, pestis minor, may be, and probably is, a disease quite apart. It consists of a prevalence of non-venereal buboes which, although noted during, before, or after epidemics of plague, may exist independently of the more severe illness.

The Lymphatic System.—Although plague is frequently termed "bubonic plague," buboes are by no means invariably present. In 73 per cent of the cases, however, they are readily detected in one or more parts of the body in almost every epidemic. Visible swelling of the glands may usher in the disease, may appear during the first twenty-four hours, may defer its appearance until the fifth day, or may never become evident. The groups of glands attacked in order of frequency are, the inguinal (vertical and oblique), the axillary, and the cervical; internal glands are also frequently involved.

Buboes develop with amazing rapidity; in a few hours they may increase from the size of a hazel nut to a pigeon's egg, and in the course of a day or two become as large as an orange. The inflammation extends rapidly to the periglandular tissues, causing œdema, subcutaneous hæmorrhage, and finally suppuration of the tissues around. The skin becomes raised, red and œdematous; the subcutaneous tissues become infiltrated, widely obscure the glandular swelling and cause extensive discoloration and induration. If the gland is deep-seated, pain is seldom complained of, unless firmly pressed upon; but the patient maintains the limb in that position best calculated to relieve tension. In 90 per cent the buboes suppurate, the result of a mixed infection with pyogenetic organisms;

the skin dies, and a slough, several inches in diameter, separates, exposing a deep, rugged cavity, discharging pus, and presenting in many instances the necrosed gland at the bottom of the space. As a rule sloughing of the cutaneous structures takes place from the tenth to the fourteenth day. Buboes which do not suppurate retain a well-marked induration for some time and disappear slowly. The presence or absence of buboes in no way affects the mortality.

Digestive system.—It would seem that in a certain proportion of cases the gastro-intestinal tract is the seat of acute and primary symptoms, more especially in instances in which buboes are not a prominent feature. The lips become speedily dry and cracked ; the tongue is at first red at tip and edges, and covered on the dorsum by a fur which changes from a grayish-white to a mahogany-brown or even black crust. The tongue appears swollen and indented or shrivelled and fissured. The mucous membrane of the mouth and fauces are unnaturally dry and redder than usual, there is great thirst at the onset, loss of appetite, and at times persistent vomiting of a watery, bilious, or coffee-ground fluid. The bowels during the acute illness are usually constipated, the fæces being hard, dark yellow or brown in colour, and later, loose dejections of a mustard colour occur, with occasionally blood and mucus in the stools.

The liver is often enlarged, and the *spleen* always so. It is seldom that pain can be elicited over either by percussion or palpation.

The respiratory tract.—Although a pneumonic variety of plague prevails, more especially during certain epidemics, the lungs in the ordinary type of plague show but few symptoms of being affected. Evanescent patches of congestion occur, which seem to come and go according to the position of the patient. In some 10 per cent of cases a bronchial catarrh supervenes and occasionally the sputum is bloody. The purely pneumonic type is characterised by the usual signs and symptoms of lobar pneumonia and is exceedingly fatal.

The heart and circulation.—The pulse at the commencement of the illness is full and tense as a rule, and at times irregular. As the strength fails the pulse becomes quick (140), feeble, and fluttering. Percussion frequently reveals the right side of the heart to be dilated, and systolic cardiac murmurs over the apex may be said to be common. With these exceptions heart lesions are extremely rare.

Hæmorrhages from one or other of the mucous surfaces, or into the skin, are common, and may appear early in the disease.

The urinary system.—The urine, during some of the recorded epidemics, remains, as a rule, unaltered, but in others marked abnormalities are met with. During the 1896 recrudescence in Hong-Kong, Wilm states that, in 95 per cent of the cases, the urine at the outset of the disease contained albumen, and in many instances indican. Suppression of urine is a frequently observed condition at the commencement of the illness, but with the decline of the fever, the quantity becomes normal and the albumen disappears, although, on the other hand, albumen has continued to appear in the urine for months subsequently. Granular casts and red blood corpuscles are frequently found microscopically.

The nervous system.—Plague is associated with a peculiar mental state. When first seized the patient may become wildly delirious. The usual form it takes is that he rushes from his room to the verandah, or into the street, but the will power soon falls into abeyance and he can assign no reason for his act when interrogated. Instead of furious delirium, or subsequent to it, the patient may be apathetic, listless, and but semi-conscious of what is said to him or what goes on around him. His features become expressionless, and when spoken to he turns towards the speaker with a dazed look, his gaze resting for a moment, and then by feature, voice, or movement it is apparent he is but semi-conscious. In children muscular twitchings and convulsions are frequently seen.

Convalescence.—A slow recovery is the rule after plague. It is usually two or three months before the patient's strength is fairly restored. Relapses of the nature of fresh adenitis, carbuncles, abscesses, pneumonia, nephritis, meningitis, keratitis, and various forms of paresis, although seldom fatal, delay complete recovery.

Recurrence.—There are but few examples of recurrence. In the experience of the writer but one case is known. A nursing sister in Hong-Kong recovered from a severe attack of plague in Hong-Kong. Two years after she had a second attack, from which she also recovered.

Diagnosis.—When, during an epidemic of plague, a patient is found with fever, a dazed appearance, a furred tongue, when he maintains his limbs in a position to afford relief from pain, and when in the groins, axilla, or neck enlarged and tender glands are found, a diagnosis of plague may be made. Mistakes are, however, possible, although not frequent. One of the most marked occurred to the writer. During the 1894 epidemic in Hong-Kong the writer was called to see a Parsee who had high fever, great thirst, a coated tongue, vomiting, and enlarged and tender groin glands. A diagnosis

of plague was made, the conclusion being no doubt contributed to by the fact that on the previous day a Parsee had died of plague in the same house. The diagnosis, however, was wrong, as subsequent examination of the man's blood showed that he was the subject of filaria. The only evidence to be relied on is the presence of the plague bacillus in the blood or the secretions of the patient.

Morbid anatomy.—In bodies of persons dead of plague rigor mortis sets in early, and is quite moderate in degree. The *skin* occasionally shows petechiæ, carbuncles, and hæmorrhage into the subcutaneous tissues.

The lymphatic glands.—Almost every lymphatic gland in the body may be found to be swollen and hyperæmic. The most intensely affected glands are of a deep violet colour throughout, or flecked by white foci of purulent matter. Around the glands the tissues are matted together, and a serous, sero-sanguineous, or purulent fluid extends widely at times into the neighbouring structures. It is usual to find chains of enlarged glands matted together, and in the groin they may be found extending upwards beneath Poupart's ligament to the iliac fossa, and even to the lumbar and retro-peritoneal glands generally. The mesenteric glands are frequently found affected, although no lesion is to be met with in the intestine.

The heart.—The pericardium occasionally shows petechial or ecchymosed spots, but the pericardial fluid is not abnormal. The heart muscle, when cut into, appears towards its inner aspects pale and soft, and the fibres exhibit a cloudy appearance or fatty degeneration. The right side of the heart and the great venous trunks of the thorax and abdomen are to be seen distended with dark fluid blood. *The lungs.*—The lower lobes of the lungs especially are, as a rule, congested and œdematous; pneumonia occurs in a certain number of cases, and much more in some epidemics than in others. The mucous membrane of the respiratory tract seems affected by an œdematous condition of the submucous coat with occasional petechiæ. The pleuræ are occasionally ecchymosed, but the pleural fluid is usually unaltered in quantity or consistence. The *stomach* contents are small in amount, and of a dark-brown colour. The longitudinal ridges present injected crests and a pale grayish-white colour in the depressions; multiple small hæmorrhages into the coats of the stomach are fairly constant. The *intestine* is usually hyperæmic throughout; the mucous coat presents small hæmorrhages and ecchymosed spots; the solitary glands are swollen; Peyer's patches are enlarged and raised, and are frequently the seat of

hæmorrhages or ulcers. The mesentery frequently contains extensive extravasation of blood; it is, in the majority of cases (60 per cent, Wilm), studded with enlarged glands of various sizes; and, as in other parts of the body also, hæmorrhages occur around the glands. The intestinal and mesenteric lesions are always most marked in cases in which external buboes are not met with. The *liver* is slightly enlarged, firm, and on section of a whitish-pink tinge with, at times, small hæmorrhages beneath the capsule. The gall bladder is fairly full in all cases, and tightly distended in many cases. The *spleen* is enlarged to as much as twice or more ts natural size; beneath the capsule hæmorrhages are common; the consistency varies, being at times firm, at other times quite soft and diffluent. The *kidneys* are congested; the stellate vessels are pronounced; and the parenchyma is in a state of cloudy swelling. Around the kidney the loose connective tissue is the seat of large extravasations of blood which frequently extend down into the pelvis. The pelvis, the ureters, and the bladder contain small coagula of blood. The *brain*.—The only changes met with are occasionally œdema of the brain substance with œdema, congestion, and small ecchymoses in the pia mater.

Prognosis.—The prognosis of bubonic plague is bad in the extreme; neither age nor sex is exempt, nor do either avail in preventing a fatal issue.

Persons living in insanitary abodes, where over-crowding and insufficiency of food prevail, are most liable to infection. Europeans in tropical countries, no doubt on account of their superior housing and mode of living as compared with the natives, seem to enjoy a certain immunity. Race may have something to do with immunity. Of the seven Japanese doctors engaged in scientific work during the plague in Hong-Kong three contracted plague, whilst of eleven British doctors engaged in treating plague patients not one caught the disease. In Egypt (1899), however, the residents of European extraction seemed as liable to the disease as the native Egyptian. This is due in all probability to the fact that many of the former live after the manner of the native Egyptians.

A bad prognosis is indicated when high fever appears early, when severe epigastric pain and vomiting prevail, when the urine is suppressed, and when buboes rapidly develop with extensive subcutaneous hæmorrhage. A better prognosis is justifiable when the initial temperature rises gradually, when buboes but slightly or very gradually develop, when the patient survives the sixth day, and when the urinary secretion remains normal.

Mortality. — The death-rate amongst the Chinese, treated according to native fashion, numbered about 95 per cent (1884). In European hospitals the mortality was less by some 15 per cent. Death in 70 per cent of the cases occurs during the first six days of the illness, but it may be delayed to the second, third, or, in rare cases, to the fifth week.

Europeans stand a better chance of recovery, some 50 per cent only of those attacked dying. Death may suddenly occur any time after the onset; convulsions or a comatose state may supervene early in the disease; or, with signs of deep nervous depression, the patient collapses. Later, death seems to result from exhaustion, the result of a pyæmic condition.

Prophylaxis.—Seeing that rats and mice are the animals which convey plague, and by which human beings become affected, their destruction *before* a threatened invasion of plague is an absolute necessity if the disease is to be averted. Should, however, plague develop it is necessary to isolate the sick, segregate those who have lived with or near them, and thoroughly disinfect or destroy their houses, furniture, and clothing, whilst at the same time war is still waged against the rat. Special prophylaxis may be obtained by inoculation with one of the several "sera" prepared for the purpose. Of these Haffkine's is the one which seems to have stood a practical test. Haffkine found different media to afford rich cultures of plague bacilli. The virulence of these was such that one or two minims were sufficient to kill the largest rodents. To lessen the virulence Haffkine resorted to destruction of the bacilli by heat, but the liquid thus deprived of its bacilli proved to possess but slight powers.

"In order to accumulate for the plague prophylactic a large amount of extra-cellular toxins, the bacilli are cultivated on the surface of a liquid medium, where they are suspended by means of drops of clarified butter or of cocoa-nut oil. The bacilli grow down in long threads into the depth of the liquid, and produce what we have termed a stalactite growth in broth, an appearance singularly peculiar to this microbe, and which, I hope, will be, till further discovery, accepted as the exclusive diagnostic feature of this microbe. The products of their vital exchanges—the toxins—are secreted by the stalactites into the liquid and accumulated there. The growth is periodically shaken off the drops of oil, after which a new crop appears underneath the surface of the liquid" (Haffkine on *Preventive Inoculation*). In this manner the bodies of the microbes collect at the bottom of the cultivation vessel, and the liquid

around becomes permeated with toxins. The process is kept up for five or six weeks, when "the bodies of the microbes become extremely deteriorated." In order to render harmless the inoculation of the virus thus prepared, Haffkine determined to kill the microbes by heating the whole up to 65° or 70° C.

The minimising effect of the prophylactic thus prepared by Haffkine was first tested on rabbits, and its powers of protection proved. Then the perfect harmlessness of the inoculation was demonstrated on Haffkine himself and a number of Europeans in Bombay who submitted to the inoculation. Many thousands of persons have been "protected" by this prophylactic, and the question now is not does the fluid procure immunity, but only how long does the conferred immunity last. As a temporary expedient the Government of India grant certificates entitling inoculated persons to exemption from plague rules for six months. In all probability this time will be extended as experience aids theory in the matter.

The dose of prophylactic administered is usually three cubic centimetres. The operation is followed by slight fever, with headache, nausea, loss of appetite, lassitude, and swelling at the seat of puncture. In two to three days all feeling of discomfort subsides.

Treatment.—In plague, perhaps more than any other disease, symptoms have to be treated as they arise. Calomel in 10-grain doses, followed by a saline purge, may be given in the initial stages. The rationale of this treatment is founded upon the fact that constipation usually prevails, that the conjunctivæ are yellow, the gall bladder full, and that the bacilli are naturally eliminated by the bowel. Instead of calomel a continued action of the bowels may be kept up by 2-drachm doses of sulphate of magnesium twice or thrice daily. When, in the later stages, diarrhœa occurs, appropriate remedies are demanded should it prove excessive. High temperature is best combated by phenacetin in 5 to 10-grain doses, repeated as required, and by the wet pack. To calm the delirium, an ice-bag to the head is to be applied, and narcotics employed. Of these morphia (gr. $\frac{1}{8}$), hyoscine ($\frac{1}{100}$th gr.), may be administered hypodermically, or bromides given internally. The practitioner, however, must devote his attention to combating heart failure; alcohol, ammonia, with or without digitalis, strychnine, hypodermics of ether and camphor are the cardiac stimulants mostly in vogue. Carbonate of ammonia in 5-grain doses, combined with decoct: cinchonæ co. ℥i every four hours is a convenient formula, the more specific drugs being administered when urgent symptoms arise. When

pneumonia or bronchitis is present expectorant remedies are to be employed. Two-grain doses of carbolic acid are recommended.

Gland swellings are dealt with according to their stage of development. When just formed glycerine and belladonna is a favourite application, and liniment of iodine may be painted on the skin over the bubo, or the substance of the gland is injected with pure carbolic acid, or a preparation of corrosive sublimate and iodide of potassium. When the glands soften and threaten to suppurate wet compresses or poultices are applied in a conventional way; but, finally, the abscess has to be opened, the gland removed, and the abscess cavity packed with antiseptic dressing.

Yersin introduced a curative preparation derived from the serum of horses. Successive horses were inoculated, and the potency of the fluid reduced to a form in which it could be safely introduced into the human body. The Pasteur Institute in Paris has elaborated Yersin's method, and the report of Professor Calmette as to the efficacy of this preparation in Oporto is most encouraging.

Quarantine.—The ordinary rules of quarantine are applicable in plague. It seems to be based on sufficiently widespread observation that incubation is a matter of five days, and that in the cargo of ships the bacillus can survive for a few days only. An individual who has recovered is considered as being capable of communicating the disease for three weeks after the subsidence of the acute symptoms, and isolation of the patient should be maintained for at least a month.

JAMES CANTLIE.

RELAPSING FEVER

SYN. FAMINE FEVER

Relapsing fever is an infectious disease caused by the presence of a micro-organism—the *Spirillum Obermeieri*—in the blood. Epidemics were frequent in Ireland and Scotland during the early part of the century; of late years the disease has rarely appeared in the United Kingdom. The poor and destitute are the principal sufferers, and, like typhus fever, epidemics have been most prevalent during times of famine. The majority of cases occur in patients between the ages of fifteen and twenty; children under five years

of age are rarely attacked. One attack confers a very limited protection against future invasion. The contagion is usually conveyed directly from patient to patient, less frequently by means of fomites.

Period of incubation.—The incubation period varies between one and twenty-one days. In monkeys the first symptoms appear from thirty hours to five days after inoculation.

Clinical course and symptoms. — The disease takes a characteristic course, divided into the following stages:—An attack of fever lasting a week or thereabouts; an intermission of about a week, during which the patient is free from symptoms; a second attack of fever, the relapse, of some three days' duration.

The attack begins suddenly with a rigor or shivering, the temperature quickly running up to between 102° and 106° F. With the rise of temperature the usual symptoms of fever supervene, thirst, headache, loss of appetite, etc. Severe pains in the back and limbs are often prominent symptoms. In spite of the high temperature, delirium and other mental disturbances are uncommon. The skin becomes of a yellow tint, and there may be distinct jaundice, with bile in the urine, the stools being of normal colour. The liver and spleen, especially the latter, become enlarged and tender. There is often vomiting, sometimes diarrhœa. The pulse is increased in frequency out of proportion to the gravity of the case; it may be as high as 140 or 160 without necessarily indicating danger. The respirations are hurried, and there is often a distressing cough, with râles and rhonchi in the chest. The urine may be albuminous. In a small proportion of cases a transient rash, consisting of minute rose spots smaller than those of typhoid fever, appears over the trunk and limbs.

After these symptoms have continued for about a week the attack terminates by crisis, the temperature suddenly falling to a degree or two below normal. The onset of the crisis may be ushered in by profuse sweating, by diarrhœa, or by hæmorrhage from the nose, bowel, or uterus. After the crisis all the symptoms rapidly subside, and the patient soon feels so well that he is with difficulty convinced that the disease is not yet over. The period of intermission continues for about a week; then the relapse sets in, the temperature again rises, and the original symptoms recur. The relapse lasts for some three days, and ends, like the original attack, by crisis. In the majority of cases the disease is now over, but second, and even third, relapses, with intervening intermissions, have been known to occur. In rare instances there is no relapse,

the patient recovering after the subsidence of the primary fever. Convalescence is always slow and tedious.

Such is the usual course of the disease; several **complications** may, however, arise. The most important are: collapse, generally setting in about the crisis; severe diarrhœa; purpura with hæmorrhages into the skin and from the mucous membranes; suppression of urine; and pneumonia. Any of these conditions may prove fatal. The pains in the limbs may be very severe, and may continue during the intermission and after the relapse. Bronchitis is sometimes of sufficient severity to rank as a complication. In some epidemics ophthalmia has been common in the early days of convalescence; the inflammation starts in the ciliary region, and ultimately may involve all the structures of the eye; permanent blindness may ensue, but fortunately both eyes are seldom affected. Parotitis was frequently observed in one epidemic in Russia. Pregnant women almost invariably abort when attacked with relapsing fever.

The Spirillum Obermeieri, often in large numbers, is present in the blood during the febrile stages. During the intermission it disappears from the blood, and probably collects in the spleen.

Pathology.—The spirilla are fine corkscrew-shaped bodies with pointed ends, twice to five times as long as the diameter of a red blood corpuscle. They are actively motile, and retain their motility from several hours up to as long as fourteen days after removal from the body, according to the temperature at which they are kept. Attempts to cultivate them outside the body have hitherto failed; so that we still lack the absolute proof that they are the cause of the disease, although there can be but little doubt that this is the case. The disease has been conveyed both to the human being and to monkeys by the injection of blood containing the spirilla. In monkeys the disappearance of the spirilla from the blood during the intermission has been proved to be due to their accumulation in the cells of the spleen. We know nothing definite about the mode of multiplication of the spirilla or of their life history outside the body. From analogy with the malaria parasite, it is probable that the period of fever corresponds to a particular stage in the development of the spirilla, and that other stages take place during the intermission. As the spirilla are not found in the secretions or excretions, it is difficult to explain the conveyance of the disease from patient to patient. There is, however, some experimental evidence of conveyance by means of insects, which would be quite compatible with the habits of the patients among

whom the disease is most prevalent. It is not improbable that the organism may ultimately be found to belong to the Protozoa.

Diagnosis. — Relapsing fever may be mistaken for typhoid fever, smallpox, typhus, influenza, or Weil's disease. The onset of typhoid is gradual, while that of smallpox, typhus, influenza, and relapsing fever is sudden. Typhoid fever can be distinguished by the long duration of the pyrexia; smallpox and typhus by the appearance of the eruption on the third and fifth day respectively; influenza by the absence of enlargement of the spleen and liver; and Weil's disease by the absence of severe nervous symptoms. In doubtful cases the diagnosis can be cleared up by placing a drop of the blood under the microscope and examining for motile spirilla. If the blood cannot be examined fresh, a cover-glass preparation should be made by allowing a thin film of blood to dry on a cover-glass. The film is fixed by passing the cover-glass rapidly through the flame, the hæmoglobin is extracted with 1 per cent solution of acetic acid, and the spirilla stained by immersion for a few minutes in one of the aniline dyes.

Prognosis.—The fatality of the disease, according to Murchison, is 4 per cent. Most of the fatal cases occur in patients over thirty; in patients below this age the fatality is only 0.5 per cent.

Post-mortem appearances.—The spleen is large and soft, with yellow areas the size of a horse-bean scattered throughout its substance. These areas, which consist of necrosed tissue, contain a large number of spirilla. Rupture of the organ, with escape of blood into the peritoneal cavity, has been recorded. The liver is enlarged; under the microscope its cells show cloudy swelling, and sometimes a small celled infiltration around the portal veins. The kidneys exhibit cloudy swelling of the epithelium, coagulation casts in the tubules, and perhaps an accumulation of small cells in the interstitial tissue. Fatty degeneration occurs in the muscle of the heart and in the voluntary muscles.

Treatment.—The patient should be isolated and kept in bed until convalescence is well established. The various symptoms must be treated as they arise; pyrexia by cold sponging; suppression of urine by poultices and dry-cupping to the loins; collapse by stimulants; diarrhœa by opium and astringents; ophthalmia by the instillation of atropine and by the application of leeches to the temples. Murchison recommended the routine administration of such drugs as acetate of potash and digitalis, with the object of preventing suppression of urine.

J. W. Washbourn.

YELLOW FEVER

A miasmatic contagious disease, caused by specific microbic infection and characterised by an acute febrile paroxysm, followed by pathognomonic symptoms indicative of toxæmic jaundice, with renal, gastro-intestinal and hæmorrhagic complications. It occurs in endemic form in some areas, elsewhere in epidemics.

Geographical distribution.—Its endemic areas are a few sea-coast towns in the West Indies, Mexico, Brazil, and Gulf of Guinea, notably Vera Cruz, Havana, Santiago de Cuba, San Domingo, and Rio de Janeiro. Epidemic outbreaks are of frequent occurrence in populous centres in communication with these cities, but rarely extend far inland, or to high altitudes, or where the temperature is below 75° F. and the humidity low. Outbreaks do occur, however, at high altitudes and in temperate zones. Arid and sparsely populated districts do not suffer. Asiatic and other Eastern countries are, as yet, exempt, but, given the necessary conditions, any populous centre may become attacked and form a fresh endemic area. Thus Rio de Janeiro, which was first attacked in 1849, has never since been free.

The American Atlantic littoral between 35° S. and 45° N. latitude, and Sierra Leone, Senegal and Gambia in Africa, have experienced frequent outbreaks. South-western Europe suffered severely at the end of the eighteenth and beginning of the nineteenth century, Gibraltar losing nearly 6000 persons, or more than one-third of its total population, during an epidemic in 1804. Another severe epidemic occurred there in 1828, and minor outbreaks in 1813 and 1814. Since 1828 European outbreaks have been unfrequent, and, with the exception of an epidemic in Lisbon in 1856-57, insignificant. They occurred at Brest, 1856; St. Nazaire, 1861; Swansea, 1865; and Madrid, 1878. The Swansea outbreak caused fifteen deaths, all of persons in direct or indirect communication with an infected vessel from Cuba; in the Madrid outbreak thirty-five died, all in a locality where soldiers, recently returned from Cuba, lived.

Seasonal prevalence.—In endemic areas north of the equator seasonal activity commences in June, is at its height in July, and continues with little diminution till December. The disease is less active from January to May. In Rio these conditions

are reversed. In epidemic zones, outbreaks usually last three months, and are generally confined to periods of tropical heat, but their duration varies and is influenced by other than seasonal factors.

Influence of race, age, and sex.—No individual of any race can claim immunity except by previous attack. Negroes, Moors, Arabs, Chinamen, have all suffered on first coming into endemic or epidemic areas. Negroes are apparently immune in the endemic zone or where epidemics are frequent, but this is attributed to attacks in childhood, probably unrecognised. On the other hand, susceptibility to and severity of attack are much greater in white than in coloured races, and in northern than in southern Europeans. New arrivals in endemic areas are specially susceptible, but susceptibility is not necessarily lessened by prolonged residence.

Age and sex influence severity, but not susceptibility, children suffering mildly, and females less severely than males.

Bacteriology.—In 1897 Sanarelli obtained pure cultures of a specific bacillus, *bacillus icteroides*, in the capillaries of the liver and kidneys, never in the digestive tract, of persons dying in the earlier stages of yellow fever. In later stages he found the body invaded with intestinal and putrefactive microbes and the bacillus icteroides incapable of detection. Outside the body, the growth of this bacillus is specially active in the presence of moulds, of which it appears to be a saprophyte, and it presents diagnostic growths on culture media. Sterile cultures injected into men and animals had steatogenous, emetic and hæmatolytic effects, resembling attacks of yellow fever. The conditions favourable for conservation of the bacillus are humidity, warmth, darkness, and want of air. It lives long in sea-water, resists drying, but is rapidly killed by solar rays. Others have described specific microbes, but their conclusions have been rejected. Sternberg failed, after careful investigation, to detect a specific microbe, but notices the invasion of the body by intestinal bacilli. The features of Sanarelli's bacillus explain, to some extent, the fact that infection is specially liable to persist in old wooden hulks and in dirty, dark, ill-ventilated ships and dwellings of tropical sea-coast towns. Insanitary surroundings are necessary for the propagation of the disease. Clean, well-paved, well-drained cities suffer slightly; those with reverse conditions severely. Moist soil, polluted with fæcal matter, forms the best nidus, and a system of cess-pits in the endemic zone favours endemicity. The mode of entrance of infective material into the body is uncertain. Evidence of infection by the digestive tract is

negative. Air convection and inoculation by stinging or biting insects are probable. Bedding, clothing and discharges from patients, ship's cargoes, etc., are regarded as the media of conveying, and polluted soil as the medium of propagating the disease, the requirements for the development of an epidemic being: (1) the introduction of infective material by sick persons, fomites, ships, etc.; (2) favourable conditions, such as polluted soil, warmth, and moisture; and (3) a community of susceptible persons. It is not directly infectious from person to person, and one attack usually confers immunity.

The minimum **incubation period** is one day, the maximum five. Usually it is two to four days. An apparent ten days' period has been noted, but records of longer periods are involved in fallacies.

Clinical history and symptoms.—There may be malaise before onset, but the attack is usually ushered in by sudden rigor with rapid rise of temperature to 103° or 104° F., and of pulse to 110 or 120, and by severe orbital and lumbar pain. This febrile paroxysm lasts two to five days, during which the temperature shows no marked rise or fall, but the pulse-rate steadily declines. The skin is usually dry, and there are anorexia, thirst, and restlessness. The patient feels and looks very ill. The face is turgid and the eyes characteristically suffused. There is much epigastric tenderness with vomiting, at first of the contents of the stomach, but, later, of bile, gastric secretions, and mucus. On the third or fourth day, seldom later, rapid defervescence sets in, the pains disappear, the body becomes cool and moist, the pulse slows to 40 or even less, and a stage of calm, with a sense of comfort and well-being, ensues. This is deceptive both to patient and physician, and requires careful management. In a few hours pathognomonic symptoms develop, more or less rapidly, according to the severity or otherwise of the attack. Yellowness of the conjunctivæ, gradually extending to face and body, diminished secretion of urine, albuminuria, and an abnormally soft, slow pulse are invariably noticed early, along with discomfort in the epigastric region. In mild cases no further symptoms may develop, and on the fifth or sixth day they disappear and the patient rapidly convalesces. In severer cases the icterus deepens and extends rapidly, the urine becomes scanty, loaded with albumen and casts, or totally suppressed, and active delirium, convulsions, and coma may ensue, although in other cases the mind may remain clear throughout. Lumbar pains return, abdominal discomfort increases,

vomiting becomes more frequent, at first of blood-stained or "coffee-ground" matter, but eventually quantities of altered blood, constituting "black vomit," may be ejected, and diarrhœa with tarry stools may set in. The temperature rises or the body may remain cold and clammy. Blood oozes from the lips and nostrils, and occasionally from other mucous orifices. Sordes accumulate, the pulse becomes feeble and slower, and a "typhoid state," with peculiar cadaverous odour, ensues. Should recovery take place, the symptoms gradually disappear about the tenth day, but convalescence may be complicated by boils, abscesses, parotitis and hepatitis. In fatal cases death is most frequent on the fifth or sixth day from anuria and coma, or from hæmorrhage and exhaustion, but it may occur early during the febrile paroxysm and before pathognomonic symptoms are prominent. It rarely occurs after the tenth day. Recurrence of the febrile paroxysm in the stage of calm, or of the more severe symptoms during convalescence from acts of indiscretion is not uncommon, especially in mild cases, and such relapses are very fatal.

Diagnosis.—The febrile paroxysm resembles the onset of small-pox, dengue, or an attack of malarial fever. During an epidemic of yellow fever the appearance of the face, the suffused eyes, epigastric tenderness and severe lumbar pain should be sufficient for early diagnosis, and absence of eruption or splenic enlargement and tenderness should positively exclude eruptive or malarial fevers. The steady decline of pulse-rate from the first day, irrespective of a stationary or rising temperature, the appearance of albuminuria and icterus on the second or third day, are positive signs of yellow fever. Later, anuria, epigastric discomfort and black vomit, tarry stools and soft slow pulse form a group of symptoms which are unknown in other diseases, and should render the diagnosis complete, although in mild cases many of these symptoms are absent, and, even in fatal cases, not necessarily present. Quinine checks malarial but not yellow fever, and, although its use in diagnosis is historical, it is deceptive, on account of the defervescence that takes place naturally about the third day in the latter disease. Serum diagnosis may prove valuable, recent experiments showing that the serum of yellow fever patients causes agglutination in cultures of the *bacillus icteroides*.

Prognosis.—An initial temperature of 106°, or even of 108° F., has been noted occasionally, and is always fatal; and the rule is that the lower the initial temperature the milder will the case be. In favourable cases the urine is scantiest on the third day, and

then gradually increases; in unfavourable cases the reverse occurs, and, if anuria sets in, death almost invariably ensues. Delirium and coma, and, to a somewhat less extent, black vomit are also usually fatal symptoms. The influence of race, age and sex, and also of relapses, has already been indicated. A previous history of alcoholism is specially unfavourable, as is also a high degree of albuminuria. An average case mortality is 30 per cent, but the ratio varies widely in different epidemics.

Pathological anatomy.—The body is stained yellow, blood trickles from and is caked about the mucous orifices, and there is early discoloration from purpuric spots or hypostatic congestion. The yellow staining is due to altered blood pigment and, unless associated with biliary jaundice, is mottled rather than uniform, and is specially marked on dependent parts and where there has been pressure. Immediately after death a high temperature of 108° to 110° may be noticed. Cadaveric rigidity sets in early, blood coagulability is diminished, and urine found in the bladder is loaded with albumen. The liver, except in the earlier stages, when it is engorged with blood, has a characteristic dry yellow or yellowish-brown wash-leather appearance, due to fatty degeneration of its cells, but is seldom contracted unless there is concurrent cirrhosis from alcoholism. The stomach is generally full of disintegrated blood and its mucous membrane congested and ecchymosed. The condition of the small intestine is similar, but the large intestine frequently presents no abnormality. In the kidneys hyperæmia in the early stages and, later, hæmorrhages beneath the capsule and in the cortical substance are noted, and the tubules present, microscopically, the appearances of acute desquamative nephritis, with fatty degeneration of their epithelium. The serous cavities usually contain some yellow-stained fluid and the other organs hæmorrhagic infarctions or ecchymoses. No changes have been noticed in the spleen.

Treatment.—No drug cure is known, and active medication must be avoided. The treatment should be on general principles and symptomatic. Sternberg recommends that three tablespoonfuls of a mixture containing 150 grains of soda bicarbonate, and $\frac{1}{3}$ grain mercuric chloride in a quart of water should be given every hour ice-cold, to lessen gastric irritability and acidity. The bowels should be unloaded at the onset by castor oil, though some prefer calomel. Subsequently enemata only should be used. During the febrile paroxysm simple diaphoretics and sponging are best; but lowering the vital powers by cold sponging at the time of defer-

vescence must be guarded against, and, for the same reason, it is best to avoid cold baths at any period. Hot applications to the loins should be applied early. Cold-water enemata and dry cupping are also useful in relieving renal congestion. When scantiness or suppression of urine is feared, pilocarpin hydrochlorate, $\frac{1}{8}$ to $\frac{1}{4}$ grain, may be injected hypodermically. After defervescence, diffusible stimulants, especially champagne, are usually required, but some prefer digitalis and strychnine, administered hypodermically. Good nursing and careful dieting are of paramount importance. Absolute rest in bed, very little food by the stomach, and that only in fluid form, given cold, and in small quantities, are essential, especially in the stage of calm. Nutrient enemata should then be employed and gastric discomfort relieved by sinapisms. Opium must be avoided. Return to solid food must be very gradual.

Recently serum therapy has been employed by Sanarelli with some success, both as curative and prophylactic. The serum is obtained from horses or oxen prepared during a long period by inoculations of *bacillus icteroides* cultures. It is supposed to be bactericidal in action, but not a true antitoxin, and it is consequently most successful in the early stages, and when injected into veins. It is useless when anuria is present, but, in Sanarelli's experience, always prevented hæmorrhagic symptoms. As a prophylactic it had successful results when inoculated into persons living in infected areas during an epidemic.

Other preventive treatment consists in attention to general cleanliness, exposing dark corners to light and air, abatement of overcrowding and removal of causes of soil pollution. Ship epidemics may be stopped by sailing to cold latitudes; troop epidemics by moving from the infected locality. Disinfection of infected clothing, bedding and discharges, as well as of habitations, should be scrupulously and systematically carried out. Where cremation is not adopted, it is essential to fill the coffins and graves of those who have died with strong disinfectants, such as chloride of lime. Isolation of patients is practised as a matter of routine. In the war between America and Spain in 1898 the rule was to keep prisoners from infected localities isolated under observation for seven days, to disinfect all their clothing and belongings, and to burn the surface of polluted soil.

W. G. Macpherson.

WEIL'S DISEASE

In 1886 Weil (*Deut. Archiv für klin. Med.* xxxix.) described four cases of an acute febrile disease associated with jaundice, nephritis, and enlargement of the spleen. A number of cases with similar clinical symptoms have since been recorded, especially in Germany, and the name Weil's disease has been attached to the malady. It appears to be a definite specific disease, and it is probable that it was previously described under various designations.

Clinical characters.—The onset of the illness is generally quite sudden, the patient being seized with headache, pains in the calves, vomiting and diarrhœa, faintness, or rigors. The temperature quickly rises to between 102° F. and 104° F., and continues high throughout the attack, which is accompanied with the usual symptoms of pyrexia—thirst, loss of appetite, rapid pulse, furred tongue, etc.

In addition there are certain symptoms special to the disease. *Gastro-intestinal* disturbances are sometimes prominent features, the patient suffering from frequent vomiting and profuse diarrhœa. *Acute nephritis* is an early and fairly constant symptom; its presence is indicated by the appearance of albumen, casts, and sometimes blood in the urine. The *spleen* is frequently enlarged, and hæmorrhages may appear in the skin and subcutaneous tissue. The *nervous system* is often profoundly affected, as shown by headache, restlessness, and delirium. *Jaundice* is of constant occurrence; it comes on about the fourth or fifth day of the attack; bile pigment and occasionally crystals of tyrosin appear in the urine; and the stools are sometimes devoid of colour. The *liver* may become enlarged and tender.

After the symptoms have lasted about ten days they usually subside, the temperature gradually falls, and the jaundice and nephritis clear up. Convalescence is always slow, and it is some time before the patient has recovered his usual health. Relapses are by no means uncommon during convalescence; about a week after the temperature has become normal, it rises again to 102° F. or 104° F., and there may be a return of the jaundice and nephritis.

The attack does not always end in recovery; Jaeger records three deaths out of nineteen cases.

Post-mortem appearances.—The tissues are bile-stained,

and hæmorrhages may be found in the subcutaneous and subperitoneal tissue, and the endocardium. The spleen is either enlarged or normal in size. The mucous membrane of the stomach and intestines may be reddened and swollen, an infiltration of small round cells being found on microscopical examination. The principal changes are found in the liver and kidneys. The former does not show much alteration to the naked eye, except perhaps that it is a little enlarged; but microscopically profound changes are to be observed. The liver cells have undergone fatty degeneration, and areas are found scattered throughout the organ in which the structure of the lobules is lost and the cells are broken down into a granular or fatty detritus. Areas of small round-celled infiltration are also found. The kidneys are swollen and sometimes streaked with hæmorrhages; cloudy swelling and fatty changes are found in the cells, and a small round-celled infiltration is present between the tubules.

Pathology.—From this short description it will be seen that the disease resembles a septicæmia in which the effect of the virus especially falls upon the liver and kidney; the jaundice is due to the degeneration of the liver cells, and the nephritis is set up by the injury to the cells of the kidney. This view is further supported by the researches of Jaeger, who found a bacillus belonging to the Proteus group in the spleen, liver, and kidneys of two fatal cases, and in the urine of several cases during life. This group of bacilli contains several species. Some are well known as the cause of putrefaction in animal and vegetable matter; while one member—the *Proteus hominis capsulatus*—is the cause of an acute septicæmia occurring among rag-sorters in Italy, the virus being probably inhaled with the dust from the rags. There is thus good reason to believe that the proteus obtained by Jaeger (*Zeitschrift für Hygiene*, Bd. xii. 1892) is the cause of Weil's disease, and the frequent occurrence of gastro-intestinal disturbances points to the mode of infection being through the alimentary tract. The disease occurs most frequently between June and September, when putrefactive changes are at their height; one of Jaeger's patients attributed his attack to eating a bad sausage, several to bathing in foul water; and it is significant that many of the sufferers from this disease have been engaged in work at slaughter-houses and sewers. Jaeger mentioned an epidemic among fowls due to a bacillus similar to the one he found in the human cases, and he believed that the water in which his patients had bathed was contaminated with the excreta of infected fowls.

Weil's disease bears a close resemblance to acute yellow atrophy in clinical symptoms and in the changes found in the liver. In both diseases a poison causes degeneration of the liver-cells; in Weil's disease the poison appears to be the proteus bacillus; while in acute yellow atrophy the nature of the poison is unknown.

Diagnosis.—Clinically Weil's disease has to be distinguished from yellow fever, acute yellow atrophy, phosphorus poisoning, and relapsing fever. The first named malady, which closely resembles Weil's disease in the acuteness of onset, with rigors, pyrexia, and other febrile symptoms and subsequent development of jaundice, is to be recognised by a history of contagion, no enlargement of the spleen, and later by the occurrence of black vomit. A fall in the pulse-rate after the first day, notwithstanding a continued high temperature, has also been said to be characteristic of yellow fever. In acute yellow atrophy jaundice occurs for several days before severe constitutional disturbances arise, while in Weil's disease pyrexia and severe constitutional disturbances occur before the jaundice sets in. The same remark applies to phosphorus poisoning, and in this disease the history or the presence of phosphorus in the vomit will remove all doubt. Relapsing fever, especially that form which is described as "bilious typhoid," is very similar to Weil's disease, and the occurrence of a relapse in the latter renders the resemblance more striking. The presence of the characteristic spirilla in the blood in relapsing fever is the most certain means of distinction. Various forms of febrile jaundice may also be mistaken for Weil's disease.

The **treatment** of Weil's disease should be based on general principles; perhaps intestinal antiseptics, such as salol, are of benefit.

J. W. Washbourn.

ANTHRAX

Syn. Malignant Pustule, Woolsorters' Disease, Splenic Fever, Charbon

Accounts of anthrax exist from the earliest time, and there have been innumerable epidemics, destroying large numbers of herbivora, both domestic and wild, and occasionally infecting men. Sheep, horses, and oxen are especially liable to this disease, whilst carnivorous animals are but slightly susceptible. In cattle, the disease may, according to Bollinger, take three forms—(1) Respiratory. In this, the animal may become unconscious, and convulsed with rapid breathing, and die within a few hours. (2) An intestinal form, in which blood passes with the fæces; there is marked pyrexia, and sometimes convulsive movements. (3) Brawny inflammatory swellings appear on the neck and body, which are very apt to slough.

The spleen, in all these forms, is greatly enlarged and softened, hence the name "splenic fever," which, however, is less suitable for the disease as it appears in man, owing to the usual absence of any characteristic changes in the appearance of that organ. It is a specific infective disease, which is most frequently conveyed to men by handling or coming in contact with the hides, hair, or carcases of infected animals. It is due to the introduction of the *bacillus anthracis*, which multiplies rapidly at the seat of inoculation, and only after an interval of some days is distributed throughout the circulation. The rapid growth of the bacilli in the capillaries sets up numerous hæmorrhages; the bacilli may be excreted by the fæces, the bile, and the urine.

Bacteriology.—The bacilli are elongated cells 5 to 20 μ in length, and rather less than 1.5 μ broad, straight or slightly concave, and immobile (Plate II.). They multiply rapidly between the temperatures of 30° C. and 40° C., in a neutral or alkaline medium, and are ærobic. When abundantly supplied with oxygen, they form elongated threads and spore readily; but in the living body, owing to the insufficiency of oxygen, they develop but short rods, and no spores. The latter are singularly resistant to heat, and retain their vitality in the soil for long periods. When cultivated on gelatine, they liquefy the medium from above downwards, and their appearance in stab culture is characteristic.

Anthrax is met with in men as a Malignant Pustule or cutaneous infection; it occurs in those who handle hides and hair, less often in knackers or butchers who deal with carcases, and but seldom in farm labourers or shepherds who are in contact with the living animals, and is still more rarely communicated directly from one person to another. The disease is not common in England, and in London most of the cases occur in the tanyards, which are aggregated in the district of Bermondsey, and hence the great majority of those affected are admitted to Guy's Hospital, where eighty-three cases have been treated during the past twelve years, of which thirteen proved fatal, while only twenty were observed between 1873-1883.

Symptoms.—In almost every case the initial lesion is on an exposed part, such as the face, neck, or occasionally the hands, due to the inoculation of some scratch, pimple, or abrasion, which is very often produced when carrying a bale of hides. A slight amount of itching is noticed at first; a papule forms, this soon passes on to a vesicle, which is readily ruptured and soon dries up, the spot being irritable and rather painful. About the third day there is an inflammatory swelling, and soon the characteristic appearances begin to develop. They consist of a depressed black scar, surrounded by a raised ring of small vesicles, while for some distance around there is a firm œdema, which gradually becomes brawny, and spreads extensively in all directions. The adjacent lymphatic glands become enlarged and tender. If the spot be on the face, it will quickly lead to extensive œdema, sufficient to close the eyelids. The nodule does not suppurate, hence the unfitness of the name "pustule," but discharges only serous fluid, in which anthrax bacilli may generally be found. The pain is chiefly due to the tension, and is not severe. The temperature is raised. There are often symptoms of great depression with rigors, followed by vomiting, and not unfrequently delirium. Unless active local measures are adopted, the toxæmia increases, and within about four days the bacilli may become widely distributed through the system. The disease is not necessarily fatal; death may occur between the fifth and eighth days, but some intercurrent trouble, such as œdema of the larynx, which is not uncommon when the pustule is on the neck, may cause death even earlier.

The cutaneous forms of the disease may be associated with one or both of the following:—

Woolsorters' Disease.—This is the respiratory variety of the affection. It was noticed in Bradford fifty years ago, after the

introduction of alpaca and mohair, that there were occasionally deaths with pulmonary symptoms amongst the men who handled the hair, which were then inexplicable; and it is chiefly in this district that the majority of the cases of anthrax infection of the lungs have been noticed in this country.

If the fleeces of animals which have had anthrax are slightly damp, or if they are greasy owing to the natural fat or lanoline in them, there is but little dust, and but little risk of pulmonary infection. The infected hair of the camel, vicuna, llama, alpaca and horse, which have no grease, are therefore the most dangerous.

Symptoms.—These are very obscure; the patient may simply feel chilly and ill, complain of oppressed breathing and be dead within a few hours. In the less acute cases the patient may be very ill, but there are generally no marked physical signs of disease in the lungs beyond râles and rhonchi, and sputum which is blood-stained. The temperature is raised several degrees, but, in consequence of the collapse, tends to drop below normal, except in the rectum. The pulse is small, rapid, and feeble. The prostration is out of all proportion to the physical signs. Just before death bacilli can be found in the blood, but it is generally impossible to detect them at an early stage; the sputum would probably be found to contain bacilli much earlier in the disease. Those who survive a week generally recover.

Intestinal Anthrax.—Infection has been stated to occur from the meat or milk of diseased animals; but is of very rare occurrence. In this country it has only been observed associated with the cutaneous or pulmonary varieties. Besides slight pyrexia, prostration, and collapse, there will be vomiting, purging, and abdominal pain, and the dejecta will contain blood.

In these internal forms of anthrax there may be delirium, or convulsions in fatal cases, though sometimes the mental state is unimpaired.

Diagnosis.—The absence of suppuration, of any sloughing core or of severe pain, together with the presence of a central eschar, with a surrounding ring of vesicles, and the brawny œdema of the adjacent connective tissue are characteristic, and distinguish anthrax from carbuncle. The lesion is a single one, which is not the case in glanders. It is always desirable to take a drop of the serum from a vesicle, or, if this be negative, also a drop from the œdematous tissue; stain it with methylene blue and examine for the bacilli, which will generally be present; though in a few cases of undoubted malignant pustule they could not be found.

In doubtful cases, especially when there is no skin lesion and a history of exposure to the infection is uncertain, a mouse should be inoculated with a drop of the patient's blood, which, if the disease be anthrax, will prove fatal in two or three days, and the blood of the animal will show the characteristic bacilli.

Prognosis.—The mortality of cases of malignant pustule on the head or neck at Guy's Hospital is about 20 per cent, whereas when the pustule is on the hand, not more than one in ten dies. The onset of very extensive œdema in the neck adds gravely to the risk; when the pustule has been excised the œdema often subsides considerably. Hurried respiration with cough, or severe diarrhœa and vomiting are very suggestive of general infection. A very rapid, feeble pulse is of evil import. At first the bacilli are limited to within an inch or two of the seat of inoculation, but after four days they tend to be widely distributed. Towards the end, in fatal cases, the bacilli can be found in the urine, and not unfrequently in the fæces and sputum, yet this does not necessarily indicate a fatal issue, as several patients who passed bacilli in their urine for some days, or even longer, ultimately recovered. When the meninges of the brain are involved, delirium and coma with convulsions may develop. The mortality of cases of malignant pustule occurring in South America and in Africa is infinitely less than when workmen in London are infected. It is difficult to explain this, except by the large amount of meat which the former consume, and by their physical vigour and open-air life. The degree of protection conferred by an attack appears to be limited, as cases have been met with where patients have had more than one attack of anthrax.

Post-mortem appearances.—Decomposition is rapid, the skin is greatly discoloured, there is extensive œdema in the region of the pustule, and very often in the connective tissue of the anterior mediastinum. Numerous small extravasations of blood may be seen in various parts of the body, and anthrax bacilli will be found in such places. On examining small and inconspicuous hæmorrhages on the mucous membrane of the alimentary canal, on the meninges of the brain, and also on the pericardium, I seldom failed to find bacilli. Occasionally extensive extravasations of blood may take place, into or on the surface of the brain; or into the intestines. The serous cavities often contain fluid, in which the bacilli will be found.

It is rare to find evidence of pneumonia, even in the pulmonary cases, but microscopical sections will show extensive hæmorrhages, with innumerable bacilli blocking up the capillaries. Sometimes

portions of the mucous membrane of the alimentary canal will be raised up by œdema, so as to form distinct swellings; in places there will be hæmorrhages, and rarely a small central slough. The condition of the spleen varies; it is generally soft; but often it is not enlarged. The abdominal lymphatic glands are frequently swollen.

Treatment.—The essential treatment for a pustule is to remove it entirely, and, where indicated, incise the brawny tissue freely. The wound is then generally packed with iodoform, and some surgeons inject carbolic acid (ʒss. of a 2 per cent solution several times daily) into the adjacent tissue. A number of cases have also been treated with ipecacuanha both locally and internally in large doses. Although evidence has been adduced suggesting that this drug might be of value, the result of experience at Guy's Hospital has been to show that a series of cases so treated have not done better than those where it had not been employed. Up to the present time no efficient treatment by an antitoxin has been available.

Good feeding, of which meat in some form should constitute a considerable proportion, and stimulants, with quinine, are essential; many of even the most unpromising cases ultimately recover.

G. Newton Pitt.

TETANUS

Tetanus is a specific infective disease, characterised by tonic spasms, chiefly affecting the muscles of the face and trunk, usually of traumatic origin, tending, with a somewhat acute course, towards a fatal issue.

Bacteriology.—The disease is the result of infection by an organism which was first obtained in pure cultivation in 1889. The bacillus is extremely slender, with rounded ends, and varies in length from 4 μ upwards. The threads, except when very short, are motile, but after growing for about thirty hours at a temperature of 37° C. spores begin to form, the threads segment, and motility ceases. The spores which occur at the end of the segments distend them, and hence the name "drum-stick" bacillus; they are extremely difficult to destroy (Plate II.). The organism is an obligate anærobe, *i.e.* it requires an atmosphere free from oxygen for its full development,

otherwise the virulence of the poison produced is greatly diminished. It grows freely between the temperatures of 14° C. and 42° C., especially in a medium containing 2 per cent of grape sugar. In a stab culture it liquefies gelatine. Owing to the resistent nature of the spores a pure culture may be obtained by raising a mixed growth to a temperature of 80° C. for an hour, which is sufficient to destroy the other organisms.

The tetanus bacillus is abundant in garden earth, in dust, and in excrement, especially in that of horses, but, fortunately, its virulence is feeble where it has grown in the presence of air.

The conditions required to produce tetanus experimentally are found to be somewhat complex. If an animal be inoculated with tetanus bacilli, there is no local suppuration, and unless the growth be an exceptionally virulent one, no further symptoms may result, as the tissues appear to be capable of destroying the organism. To produce tetanus, this protective mechanism must be hindered, which may be done in several ways, either by introducing at the same time some tetanus toxin; by traumatic injury to the tissue; or by a mixed infection with pyogenic cocci, which, by absorbing oxygen from the tissues, enhance the virulence of the poison produced by the tetanus bacilli, and allow them to develop more freely with less interference from the living tissues.

The bacilli remain localised at the seat of inoculation, and are to be found neither in the blood nor in the other tissues. The poison is produced very slowly, but it is one of the most virulent which is known, as $\frac{1}{300}$ minim of a filtered alkaline broth culture of the microbes, three weeks old, is sufficient to kill a rabbit.

The poison can be obtained from the blood, spleen, liver, spinal cord, urine, etc., of a patient with tetanus, by precipitation with alcohol. The introduction of the toxin without any bacilli is capable of producing all the symptoms of tetanus, and hence the removal of the seat of infection so as to stop the production of the toxin has been regarded as an important part of the treatment. It has been shown that the poison has a definite affinity for the nerve cells, for if a suitable portion of brain or spinal cord be rubbed up into an emulsion with an otherwise fatal dose of tetanus toxin and injected into an animal, no symptoms of tetanus will ensue, as the poison appears to be fixed by the nerve elements. That the toxin is not neutralised is shown by the fact that if the nerve tissue be only injected close to the spot where the poison has been inserted, it does not prevent the development of the symptoms.

When an animal has been successfully inoculated with tetanus,

there is a short incubatory period, after which tonic spasms develop in the muscles near the seat of infection. These are due to the action of the poison, which appears to spread up to the spinal cord by the nerves, and, acting on the adjacent cells of the anterior horn, increases their irritability. Later on, the poison is diffused through the body by means of the blood vessels, so that all the nerve cells become subject to its influence. The spasms spread to the muscles of the face, neck, and trunk, and soon become almost universal.

Etiology.—Generally on examination a local injury can be found, which may have been a severe one, such as a compound fracture, or an operation such as ovariotomy; but in many cases there has been only some slight abrasion or a punctured wound, commonly on the feet, hands, or face, particularly in persons liable to come in contact with soil or garden mould. In some no definite injury has been noticed; these are called idiopathic, and have been especially observed in time of war, where men have been exposed to much wet and cold. Most of those cases which have been observed after parturition have been reported from the tropics. Some were premature deliveries, others at full time, but in several the uterus had been plugged for hæmorrhage.

Tetanus neonaturum occurs in new-born children in whom there has been infection of the umbilical cord, and is very prevalent in some islands, often as an epidemic.

Men are much more frequently affected than women in the proportion of about six to one; this is probably due to their increased exposure to injuries. The disease may occur at any age, more especially in the young and active; but, excluding the cases which occur within the week after birth, it is rare before the age of five years. On the whole the disease is more prevalent in hot climates.

Incubation period.—It is difficult to fix this, but in acute cases, which run a rapid course, the symptoms appear within four or five days after injury, and occasionally sooner; the interval is usually under two weeks. The interval varies with the amount of the poison introduced.

Symptoms.—Tetanus commonly commences, a few days after an injury, with symptoms of a stiff neck or of a sore throat, which are at first considered to be trivial, or the patient finds that there is a difficulty in opening his jaws owing to a tonic spasm of the masseters, whence the name of lockjaw or "trismus." In other cases the first indication is a set and aged expression, due to the contraction

of the facial muscles, so that there is a fixed smile with a great increase in the naso-labial folds, to which the term "risus sardonicus" is applied. The forehead is wrinkled and the eyes but half opened, owing to the contraction of the orbiculares oculorum. Shortly after the advent of these symptoms the rigidity increases, and other muscles, especially those of the trunk, become affected. The abdomen becomes as rigid as a board, owing to the tonic contraction of the recti abdominis; the trunk muscles become contracted, and in severe cases a more or less marked condition of opisthotonus develops, so that the patient is supported by his heels and his head: sometimes also with a lateral curvature of the spine during the paroxysms. It is a marked characteristic of the disease that, although the proximal muscles of the limbs may be affected, those of the hands and feet are neither rigid nor stiff, although tenderness and a feeling of stiffness in the region of the seat of infection may be noticed; but local spasms are generally so slight as only to be elicited by careful inquiry, the patient's first complaint being usually of the condition of his head or neck. When the initial lesion has been in the head the symptoms differ somewhat; there is some paralysis as well as rigidity of the facial muscles, and not infrequently there is marked pharyngeal spasm; such cases have been termed "cephalic tetanus."

To the condition of tonic contraction are soon superadded paroxysmal contractions, which are readily induced by the slightest movement or even by a breath of wind. These recur with increasing severity and frequency, and may be so violent as to lead to rupture of muscular fibres. Exceptionally there may be only tonic spasm or only paroxysmal contractions.

Pain is an early symptom, and in severe cases it is intense, similar to that of cramp; a very distressing pain behind the sternum is often present, and is probably the result of spasm of the diaphragm. If the patient can sleep the spasm relaxes, but in severe cases this is often impossible.

The temperature varies; in the extremely severe cases, with frequently recurring convulsive attacks, it is raised and may run up towards the end to 105° F. or higher. An analysis of the temperatures in a series of cases shows that in the more moderate, when it is only raised to 102° or 103°, there is generally sufficient local suppuration to account for this; and that when the initial seat of infection is free from inflammation the temperature may not be raised. The pulse may be rapid and is often very small.

The urine is found to be free from albumen, but there is often

a difficulty in micturition owing to the spasms not only of the abdominal muscles but probably also of those of the bladder. Constipation is common. The amount of perspiration is variable, sometimes it is excessive.

Prognosis.—The acute cases, 95 per cent of which are fatal, seldom survive seven days, and death may occur in twenty-four to thirty-six hours from the commencement of the attack. The later the onset of the symptoms the greater the probability of the case running a subacute course. Exceptionally, however, patients have died after five or six weeks, and one girl died five months after running a nail into her foot, and four months after the onset of symptoms, which throughout were never very violent. Very few of the cases following parturition or occurring in new-born infants recover. If the patient have survived ten days there is a fair prospect of ultimate recovery. This is always a very gradual process; the spasmodic attacks become more infrequent and less severe, but the tonic contraction of the muscles persists for a long time, and only passes off very gradually. The mortality of so-called idiopathic cases is about 50 per cent.

Modes of death.—In acute cases the patients may die from asphyxia due to prolonged tonic spasm of the respiratory muscles, which may remain absolutely fixed for more than a minute. If such attacks recur, the patient is almost certain to die in one of them, the pulse continuing after the respiration has ceased. In other cases, the patient gradually dies from exhaustion or from cardiac failure, the intelligence being preserved to the last.

Post-mortem appearances.—There are no constant lesions to be found. In a few cases there has been evidence of inflammation spreading up along the nerves from the seat of injury, but in many this is absent. Ecchymoses and cell-infiltration of the perivascular spaces on the surface of the brain and in the spinal cord have been noticed. Possibly with the modern methods of examination, changes may be found in the nerve cells of the spinal cord.

Diagnosis.—Tetanus has to be distinguished from the following:

Strychnine poisoning.—Here the symptoms come on suddenly, within a short period after taking the poison, and two hours after the first spasm the patient is either dead or is recovering. There are violent convulsive movements, which affect the whole body; the hands are clenched, but the jaws are affected late, if at all. The muscles are completely relaxed between the spasms. The patient may die within a few minutes of the onset of the spasms.

Hydrophobia.—In this malady the spasms are paroxysmal and

not tonic; they mainly affect the muscles of deglutition and respiration, and are induced by attempts to drink. Among other distinguishing features are the delusions and other mental disturbances which are seldom or never met with in tetanus.

Cerebro-spinal meningitis.—Tonic spasms are readily induced by movements; but the pyrexia, the optic neuritis, the vomiting, headache and stupor, suffice to distinguish.

Hysteria.—This may produce opisthotonus and trismus, but the other associated symptoms indicate the diagnosis. If there is only trismus, the onset is sudden and complete, and the neck is not stiff.

Tetany.—The characteristic and tonic contraction of the fingers at once differentiate this.

Local inflammation, such as results from impaction of a wisdom tooth, may prevent the jaws from being opened, but the masseters are not contracted, nor are there contractions in other muscles.

Any suppurating centre should always be examined for tetanus bacilli, but they are not always to be discovered, and in any case of doubt cultivations should be made, and a drop of pus or fluid should be inoculated into the root of the tail of a mouse, which, if infected, will die within three or four days from tetanus.

Treatment.—Prophylactic treatment is of the greatest importance. Since aseptic methods have come into use, tetanus has become a much rarer disease than formerly. All wounds, especially those which have been contaminated with garden soil or manure, should be thoroughly cleaned, and suppuration should be prevented when possible. In any case of tetanus any suspicious abrasion or injury should be thoroughly scraped and examined under an anæsthetic, any foreign body removed, and any inflamed or suppurating area excised when feasible. There is no justification, however, for the removal of a limb, solely on the ground that it would remove a focus of infection, as this has not led to beneficial results. It has been proposed that the wound should be dressed with a ten-volume solution of peroxide of hydrogen, and frequently bathed in it, but it is of even greater importance to keep the wound aseptic.

No more striking instance of the value of cleanliness and of the use of antiseptics in the prevention of tetanus could be afforded than that of its abolition in the year 1893 from the Island of St. Kilda. Previously, 84 out of 125 children, or 67 per cent, had died of tetanus, or, as it was called locally, of the "eight-day sickness."

Antitoxin.—Tetanus was the first disease in which the curative

effects of the injection of the serum of animals which had been previously rendered immune to the poison of a disease was thoroughly investigated. If such serum be injected at the same time, or soon after, an animal is inoculated with tetanus, its prophylactic effect is marked. When the subcutaneous injection of the antitoxin is delayed until the onset of tonic spasm, it is quite unable, if the attack is severe, to stay the progress of the disease. The serum is able to protect nerve cells from afterwards becoming affected by the poison, but it cannot counteract the poison if it have already injured the cells.

Within the past year, however, it has been shown by Roux and Berrel that if the serum be injected directly into the brain substance, even after the onset of symptoms, it is capable of terminating the spasms and of inducing recovery. Clinical experience has also already led to some remarkable recoveries following this method (*Brit. Med. Journal*, 1899, i. pp. 10, 895, and 1333). The procedure, however, is not free from danger, since one of these cases, when convalescence was apparently fully established and all symptoms of tetanus had disappeared, died eight weeks after the last intra-cerebral injection from cerebral abscess, although every care had been taken to secure asepsis at the operation of drilling the skull and injecting the serum (*ib.* ii. p. 9).

In a dubious case, before the onset of definite symptoms, the subcutaneous injection of 10 cc. of antitoxic serum, repeating this once or twice a day as necessary, will probably suffice to stay the disease. Should the symptoms be fully developed, according to present experience, it is desirable also to trephine over each frontal eminence, and with due aseptic precautions slowly to inject into the brain tissue on each side 5 cc. of serum. The injections may require to be repeated. This will prevent the cerebral cells from fixing the poison, while the subcutaneous injections will neutralise the poison in the blood. Recovery takes place slowly after a prolonged illness.

The following means, though powerless to save a patient's life if the attack is severe, are of considerable value in the milder cases in alleviating the symptoms:—

It is most important that the patient be kept quiet in bed in a darkened room, and carefully protected from every form of irritation.

Chloral, if used, must be given in large doses, and frequently repeated, 20 to 30 grains being indicated, but much larger doses have often been employed. Morphia, given subcutaneously and at short intervals, affords great relief. One-sixth of a grain of morphia was given every two hours for a fortnight to a boy under the writer's charge, with very great amelioration of the symptoms, and with

ultimate recovery. Preparations of physostigma in large doses, bromides, and other sedatives frequently repeated, have been used with some benefit.

Chloroform is required when the spasms are very severe, and when the chest has been held fixed by a profound spasm. It may advantageously be combined with artificial respiration, which is preferable to tracheotomy should the respiration cease from spasmodic fixation of the chest.

When there is a difficulty in feeding the patient, liquid food can be introduced by a soft tube passed behind the teeth, or through the nostrils, but the passage of a nasal tube into the œsophagus generally brings on an attack of spasm, so that it may require to be introduced under an anæsthetic, or rectal feeding may be resorted to.

G. Newton Pitt.

DIPHTHERIA

Syn. Membranous Croup

The disease is characterised by an exudative, or membranous inflammation of the faucial, nasal, or respiratory mucous membranes, more rarely of wound surfaces; attended, in severe cases, with profound constitutional depression, and degenerative changes in certain tissues, notably the peripheral nervous system, cardiac muscle, and renal parenchyma. These changes result from the absorption into the circulation of toxic material elaborated by a specific bacillus which is invariably present at the seat of exudation. The presence of this bacillus, which was discovered by Klebs in 1883, and subsequently confirmed by Löffler, is now held to be the only true criterion of diphtheria; although the teaching of Bretonneau, that the presence of exudation was in itself distinctive, had until recent years been almost universally accepted.

Etiology.—Though widely diffused, it is chiefly in temperate and cold damp climates that diphtheria prevails. Damp, low-lying districts, possessing a soil retentive of wet, and rich in decaying organic matter, usually show a high fatality from diphtheria, especially if subject to the continued prevalence of cold winds, coupled with a high rainfall. In this country the disease seems to have

been on the whole more prevalent in those counties lying along the east coast than elsewhere. Like enteric and scarlet fevers, the greatest incidence of diphtheria falls in the late autumn and early winter, the maximum usually being attained either in November or December, when the case mortality, too, is often above the average. The prevalence is usually at its lowest point during the summer months. It is an interesting fact that in England, at any rate, diphtheria, though formerly more frequent in rural districts, has during the last twenty years shown a constantly increasing tendency to affect the population of towns, though different outbursts are characterised by considerable variation in severity. There are good reasons for believing this to be mainly dependent upon conditions associated with the extension of compulsory education. It is now more or less endemic in most large towns.

Our views as to the part played by *drainage defects* in the etiology of diphtheria have undergone considerable modification of late. It is now very generally recognised that inadequate drainage of the surface soil, deficient scavenging, and dampness of habitation, are influences far more potent in the propagation of diphtheria than the inhalation of sewer gas, which, until recently, was universally regarded as a common source of direct infection. Now, although sewer gas can hardly be regarded as a source of direct infection—and it may be remarked that the diphtheria bacillus has never been detected in it—there is no doubt but that the health of persons who have been for some time living under its influence may become injuriously affected. Their powers of resistance become lowered, even if they do not suffer from a definite sore throat, and under these circumstances they are prone to fall easy victims to a chance infection, and contract the disease in an aggravated form. Another important factor in the propagation of diphtheria is school attendance. Not only does the herding together of a number of children under one roof for several hours a day provide special opportunities for the transmission of infection, but the potential victims are of an age at which they are very liable to take diphtheria when exposed to it, and one, moreover, at which they are very susceptible to the noxious influence of overcrowding and inadequate ventilation. The combination of the foregoing conditions, known collectively as "*school influence*," has been shown by Sir Richard Thorne Thorne to be competent to bring about a progressive increase of infectivity in a consecutive series of throat attacks; so that severe, or even lethal attacks of diphtheria may result from what originally appeared to be a trivial non-specific sore throat.

Although the part played by faulty sanitation and school influence in the diffusion of diphtheria is well recognised, the most important agent is undoubtedly personal infection. The contagium of diphtheria is readily transmissible by means of minute particles of mucus or flecks of membrane, which may be ejected from the mouth or nose by an act of coughing, sneezing, or even laughing in an explosive manner. The *infective material* may either be transmitted directly into the mouth or nose of another person, or indirectly, after complete desiccation, by means of a current of air. Infection, too, may result from the act of kissing, or from using the same pocket handkerchief, cup, or spoon. *Milk* is a frequent channel of infection. In some cases, no doubt, it becomes accidentally contaminated from a human source. The bacillus grows well in milk; in other cases, according to Dr. Klein, the milk appears to derive its infective properties from the cow itself, in virtue of the animal being affected with a disease the counterpart of human diphtheria. *Cats* are a distinct source of danger, as they are liable to contract true diphtheria, and thus transmit the disease. There is no reason to think that diphtheria is ever spread by means of an infected water supply. A person should be regarded as a possible source of infection so long as any diphtheria bacilli can be detected in the throat or secretions, nor, if practicable, should he be allowed to mix with others until the discharge from any affected surface has ceased.

Predisposition to diphtheria varies with *age*, *sex*, *state of health*, and previous attack. The influence of age and sex is shown by the table given on next page, which is compiled from the total diphtheria admissions into the hospitals of the Metropolitan Asylums Board during the ten years ending 1897.

Approximately, three-fourths of the attacks were in children under ten years of age. The same fact is apparent in respect to scarlet fever; but in that disease the incidence is greatest in the second quinquennium of life, instead of the first. One-fifth more females were attacked than males. Persons are very liable to contract diphtheria who have been recently subject to any acute disorder, especially if attended with any sore throat or nasal discharge, such as tonsillitis, scarlet fever, or measles. In this connection the influence of drainage defects and overcrowding has been already referred to. The immunity conferred by an attack of diphtheria lasts but three or four weeks in most persons, hence a relapse or definite second attack is often met with.

The **period of incubation** is frequently difficult to determine, because an exudation may have been present for several days before

AGES.	Males.			Females.			Total.		
	Admitted.	Died.	Mortality per cent.	Admitted.	Died.	Mortality per cent.	Admitted.	Died.	Mortality per cent.
Under 1 . .	239	115	48.1	196	103	52.6	435	218	50.1
1 to 2 . .	819	411	50.2	729	368	50.5	1,548	779	50.3
2 ,, 3 . .	1,101	466	42.3	1,120	440	39.3	2,221	906	40.8
3 ,, 4 . .	1,486	545	36.7	1,485	503	33.9	2,971	1,048	35.3
4 ,, 5 . .	1,423	432	30.4	1,662	517	31.1	3,085	949	30.8
Totals under 5 years	5,068	1,969	38.9	5,192	1,931	37.2	10,260	3,900	38.0
5 to 10 . .	3,978	850	21.4	4,720	1,094	23.2	8,698	1,944	22.3
10 ,, 15 . .	1,265	110	8.7	1,695	144	8.5	2,960	254	8.6
15 ,, 20 . .	497	26	5.2	817	34	4.2	1,314	60	4.6
20 ,, 25 . .	297	14	4.7	562	20	3.6	859	34	4.0
25 ,, 30 . .	182	12	6.6	405	13	3.2	587	25	4.3
30 ,, 35 . .	119	4	3.4	222	14	6.3	341	18	5.3
35 ,, 40 . .	67	4	6.0	118	5	4.2	185	9	4.9
40 ,, 45 . .	37	3	15.0	58	5	12.3	95	8	13.3
45 ,, 50 . .	19	1		34	4		53	5	
50 ,, 55 . .	15	4		14	2		29	6	
55 ,, 60 . .	6	2		15	1		21	3	
And upwards	3	2		9	4		12	6	
Grand Totals	11,553	3,001	26.0	13,861	3,271	23.6	25,414	6,272	24.7

attention is called to the throat. Symptoms of invasion often appear within thirty-six hours of infection, and though they are rarely delayed more than four or five days, a quarantine of ten or twelve days should be maintained.

For the purposes of **clinical description**, attacks of diphtheria may be conveniently divided into the five following groups :—

I. *Mild Faucial Form.*—This class of case is most common in adults, and, except for the presence of exudation, there is little to distinguish it from an attack of simple tonsillitis. The exudation is usually limited to the tonsils, which are more or less swollen, one commonly more than the other ; but a patch may form on the contiguous side of the uvula. The exudation usually takes the form of a thin, fibrinous, or cheesy-looking pellicle, of a dead white or grayish tint, lying on the surface of the tonsil, to which it is loosely adherent. In other cases the exudation occurs in one or more depressed

patches, with clearly-defined margin, resembling a shallow necrotic ulceration of the tonsils, which, like the surrounding mucous membrane, are red and angry-looking. The subjacent glandular swelling corresponds to the extent to which the tonsil on that side is involved. The pyrexia usually ranges from 101° to 103°, its degree being proportionate to amount of faucial inflammation, and slight albuminuria is common. After three or four days' appropriate treatment the exudation commonly clears, and the patient is convalescent by the end of a week or ten days.

II. *Severe Faucial Form, usually showing a tendency to extension.*—This is most common in young children, in whom the mortality is very high. The disease affects the fauces primarily, and from thence may spread to the pharynx, nares, or respiratory passages. The symptoms of invasion are in most cases pronounced; but in some patients the attack represents a progressive development of one which originally bid fair to run a mild course. For this reason no attack of diphtheria in a young child, however mild, should ever be lightly regarded. The onset is usually attended with shivering, pain in swallowing, and not infrequently vomiting, in addition to the usual signs of febrile invasion. The tonsils are much swollen at an early stage, and may almost meet in the mid-line so as to partially obscure the uvula, which is usually œdematous. Their surface is covered with thick white exudation, presenting either a glistening or dead-white appearance like that of wash-leather, and the faucial mucous membrane generally is usually of a pinkish rather than deep red colour, and slippery-looking, owing to the presence of much glairy mucus. The uvula is sometimes ensheathed with a coat of membrane, like the finger of a glove, and patches of exudation are often present on the soft palate and anterior pillars of the fauces. There is usually considerable infiltration of the subjacent glands and connective tissue, and a muco-purulent or thin straw-coloured discharge may escape from the nostrils, in consequence of the nasal fossæ having become involved in the disease. The tongue is coated with a pasty fur, and the temperature during the first three or four days is raised, perhaps, to 103° or more; but under the influence of efficient local treatment, apart from the effect of antitoxin, a rapid fall commonly occurs, even before the condition of the fauces shows a corresponding improvement. Diphtheria has no typical temperature curve, the worst cases often having a normal temperature almost from the commencement. The patient's condition becomes one of great distress, in consequence of the acute pain which constantly attends the act of swallowing food and saliva. His distress is in-

creased by reason of the nasal passages being more or less blocked; and should the disease extend to the larynx, the horrors of croup are superadded. Epistaxis, or bleeding from the margin of the faucial exudation, may occur at this stage, and the urine is usually albuminous. As the case proceeds the exudation becomes discoloured, owing to putrefactive changes, and is gradually thrown off, perhaps to be replaced by a fresh deposit. If forcibly removed, a bleeding and excoriated surface remains.

Should the patient survive, the general swelling of the parts undergoes considerable abatement by the end of the week, or a few days later, though the pulse at this stage may show distinct evidence of weakness. A superficial ulceration remains after the membrane has become detached. This soon heals, and the faucial discomfort then disappears.

Now, it by no means follows that recovery will ensue, although the patient may have progressed to the above extent. Nothing could be more fallacious; for the second week of diphtheria, especially its latter half, is the time when the most fatal development to which the patient is liable, viz. "cardiac failure," is most likely to arise, though it may not appear until a week or two later. The onset of cardiac failure is characterised by progressive enfeeblement of the circulation, and often, though by no means necessarily, there is marked dilatation of the left ventricle. The pulse becomes unduly slow, or irregular, and, though in some cases its rapidity is increased, its tension is always diminished. Incessant vomiting, increasing pallor, combined with restlessness, and sighing, or irregular respiration, are constant features. Acute pain in the epigastric or precordial region is often present, and distressing cramps in the muscles of the back and limbs are sometimes complained of. The temperature becomes subnormal, much albumin appears in the urine, which is scanty; or it may be entirely suppressed for twenty-four hours or more before death. Coldness of the extremities gradually supervenes, the collapse becomes more profound, and life slowly ebbs away, the patient usually retaining consciousness to the end. The victim sometimes lingers on for several days, but a sudden syncopic attack usually terminates the scene.

In the very worst, the so-called "malignant," attacks, the whole of the faucial structures become rapidly covered with a thick sheet of gelatinous membrane which often encroaches on the hard palate and buccal surface of the cheek. The nares, too, are blocked, and a thin blood-stained fluid exudes from the nostrils. There is much swelling of the neck, and the patient, quite unable to swallow, dies

from cardiac failure before the end of the week. The toxæmic character of such an attack is evidenced by the waxy pallor of the skin, which is early apparent, the cyanotic appearance of the lips, the staining which is seen to follow the course of many of the superficial veins, the lowness of the temperature, the cardiac depression, and the liability to some form of hæmorrhage. This may occur from any of the mucous surfaces—fauces, nares, gums, conjunctivæ, stomach, intestines, genito-urinary passages, or into the tissue of the skin. Bruising may result from the slightest pressure, or the most insignificant contusion, and is well marked round the site of a hypodermic injection. Hæmorrhagic attacks are seemingly always fatal. Death usually occurs during the course of the second week, but in the worst cases may take place earlier.

III. *Laryngeal Form.*—The air passages may be affected primarily, sometimes exclusively; but croup more often arises as a complication of faucial diphtheria, which, if mild, may have previously escaped observation. The term "croup" denotes a condition of laryngeal obstruction, whether membranous, as in diphtheria, or not. Its onset is characterised by the gradual development of hoarseness, with an ineffectual, metallic cough, and ultimately complete aphonia. After from twelve to thirty-six hours the laryngeal affection usually becomes sufficiently pronounced to be a source of actual dyspnœa. The breathing is stridulous, the child becomes restless, and is in constant terror of suffocation. Marked recession of the soft parts of the thoracic walls as well as of the lower ribs and epigastrium on inspiration is then apparent; expiration becomes attended with distinct muscular effort; cyanosis and drowsiness gradually supervene, and the child dies suffocated, unless relieved by operation. The membrane, meanwhile, usually spreads down the trachea into the bronchial tubes, often to their smallest ramifications. In favourable cases the laryngeal swelling subsides in a few days, more or less complete casts of the trachea and bronchi being at times expelled, and convalescence advances rapidly. Diphtheria, when limited to the air passages, is rarely followed by cardiac failure or paralysis. Primary laryngeal diphtheria is seldom seen in adults, and although extension to the larynx occurs in them occasionally, it rarely gives rise to obstructive dyspnœa. It may prove fatal, however, by spreading to the smaller air passages.

IV. *Nasal Form.*—The nasal passages are frequently involved in severe faucial attacks, consequently nasal diphtheria is generally regarded as a grave condition. Pure nasal diphtheria, however, is commonly a mild development, and occurs more often

than is usually supposed. Frequently, the only indications of its presence are—a thin mucoid rhinorrhœa, containing numerous diphtheria bacilli, slight soreness of the external nares, and some tenderness of the superficial lymphatic glands beneath the jaw. Occasionally shreds of membrane, or incomplete casts of the nasal fossæ are expelled. In rare instances the condition becomes more or less chronic (rhinitis fibrinosa), and the patient continues to expel casts, often of the inferior turbinated bone, every few days for several weeks, or even months, though his general health remains unaffected. The importance of the condition, however, from the point of infectivity must not be overlooked.

V. *Other Forms.*—Diphtheritic exudation sometimes occurs on the mucous membrane of other parts, viz. the cheeks, gums, tongue, lips, conjunctivæ, the external genitalia, especially in females, and on the surface of open wounds. The condition is usually associated with either faucial, nasal, or laryngeal diphtheria; but in the case of open wounds is, perhaps, more often primary. The gravity of the condition is proportionate to the amount of surface involved. Most cases of extensive wound diphtheria are fatal through cardiac failure.

Of the **complications** liable to supervene, the following list shows the percentage incidence amongst 16,360 attacks of diphtheria :—

Albuminuria	40.8 per cent.
Paralysis	19.1 „
Broncho-pneumonia . .	2.2 „
Relapse	1.6 „
Nephritis	.88 „

Albuminuria should be regarded as a symptom rather than a complication of diphtheria. It is present in more than half the number of severe attacks, and is often excessive. It usually arises towards the end of the first week, or early in the second, and, as a rule, disappears shortly after the throat is clear. Though sometimes persistent for several weeks, it does not imply any serious lesion of the kidneys.

Paralysis of diphtheritic origin varies widely both in its distribution and degree. It is rarely complete, and is usually attended with more or less sensory disturbance. It is far more common after severe attacks than mild ones. Indeed, so true is this relation, that the chance of subsequent paralysis may usually be gauged by the character, extent, and persistence of the previous exudation.

An exception, however, must be claimed in respect to laryngeal, and pure nasal diphtheria, which are rarely followed by definite, much less extensive, paralysis; and in rare instances a mild faucial attack is followed by widespread palsy. The paralysis affects young children more often than older patients, and most frequently arises during the second, third, and, more rarely, the fourth week of illness, though it may appear as late as the sixth or seventh week in exceptional instances. The part most often and, usually, earliest affected is the palate. The velum is seen to lie motionless, and its natural arch appears somewhat flattened. Its sensibility is impaired, and its reflex excitability lost. The voice, consequently, assumes a nasal quality, and the act of swallowing results in the passage of food into the nasal cavities. The ciliary muscle, next to the palate, is most likely to suffer, resulting in failure of accommodation for near vision, and consequent inability to read. Oculomotor paralysis also occurs, though less often, causing diplopia and strabismus, the external rectus being most often affected. It is frequently bilateral. Complete ptosis is rare, but a partial weakness of the levatores palpebræ can often be detected, which gives the patient a sleepy expression. Next to the palate and eyes, the legs most frequently suffer. Sensory disturbance usually appears first in the form of tingling, or "pins and needles" in the feet; or a sensation of cotton-wool under the soles, combined with numbness, or actual anæsthesia. This may spread up the legs, even to the thighs, and is almost invariably combined with loss of patellar reflex. More or less muscular weakness in the legs is usually present, but rarely complete paralysis. A loss of patellar reflex may occur apart from any indication of paralysis or anæsthesia.

In exceptional cases the arms are affected, or the muscles of the neck and trunk, the patient being then unable to sit up in bed or support the weight of his head. The diaphragm, or the intercostal muscles may become paralysed, both of which are a source of urgent danger. In extreme cases anæsthesia of the tongue and buccal surface may occur, and even blunting of the sense of smell and of taste. The sphincters are unaffected throughout. Considerable wasting of the affected muscles sometimes occurs, in degree proportionate to the duration of the paralysis. Although in the large proportion of cases recovery takes place in a few weeks, it may be several months, or even several years, before complete restoration to health is attained.

After severe attacks of diphtheria a group of paralytic symptoms of far greater gravity than the foregoing is liable to arise. During

early convalescence the paralysis of the palate may become attended with paralysis of the pharyngeal constrictors, with the result that deglutition is rendered impossible. The arytæno-epiglottidean muscles, and the adductors of the larynx are usually affected as well, and the larynx becomes anæsthetic. The patient is consequently liable to be choked by the passage of food into the trachea, or to be carried off by septic broncho-pneumonia. Vomiting, cardiac depression or irregularity, and sudden albuminuria are often superadded. These may be the result, no doubt, of cardiac failure ; but their association with the above paralytic manifestations, and the fact that recovery sometimes ensues, are strongly suggestive that some temporary disturbance of the functions of the vagus nerve, rather than myocardial degeneration, is responsible for their production.

Broncho-pneumonia in some degree is probably more common than the above record would seem to imply. Patches can almost invariably be found in fatal cases of laryngeal diphtheria, though it may have been impossible to detect them during life.

A relapse or recrudescence of the disease is liable to occur at any time after the third week, especially in cases treated with antitoxin. It is almost invariably milder than the original attack.

Nephritis is very uncommon. Though renal casts are present in all cases, hæmaturia is rare. The attack otherwise presents no special features and the patient usually recovers.

The susceptibility of the diphtheria patient to the infection of scarlet fever must not be forgotten.

Prognosis.—The death-rate in different epidemics of diphtheria is very variable. It is mainly influenced by the relative proportion of young children amongst those attacked, and the hygienic conditions under which they live.

The case mortality amongst the 25,414 cases tabulated on page 166 was 24.7 per cent, but under the influence of the antitoxin treatment (commenced in December 1894) the fatality in the hospitals of the Asylums Board has been reduced from over 30 per cent to about 15.

The most important factors in prognosis are—

1. *Character of attack.*—In laryngeal cases the prognosis is always grave, especially if secondary to previous faucial affection. In faucial attacks important indications are yielded by the extent, persistence, and character of the exudation. In proportion as the disease has spread from the tonsils on to the palate, uvula, pharynx, or into the nasal fossæ, the gravity of the attack will be greater, because a

larger surface is concerned in producing the toxin. So, too, if the exudation be unduly persistent, more toxin is produced, and relatively more absorbed. If an extensive membrane remain attached for five or six days the case at once assumes a serious aspect; if for two or three days longer, the prognosis becomes exceedingly grave. The prognostic significance of extent and persistence of membrane must necessarily be relative. The most virulent type of membrane is one which is thick and gelatinous, or sometimes distinctly fibrous in appearance, and attended with marked œdema of the mucous membrane. The least virulent is thin and friable, or of cheesy consistence, with well-defined margin, and little, if at all, raised above the surface. Between them all gradations occur. In thick adherent membranes, putrefaction occurs *in situ;* hence, fetor of the breath is a bad sign. Extensive infiltration of the deep cervical glands and connective tissue implies virulence of the local process. A normal or subnormal temperature, coupled with a feeble or rapid pulse, is indicative of toxæmia; and waxy pallor of the complexion, and the sudden onset of severe albuminuria is evidence in the same direction. Hæmorrhage from a mucous surface is usually a fatal sign, and the writer has never seen a patient recover in whom purpuric spots were observed in the skin.

2. *Age.*—The enormous influence on fatality exerted by age is well shown by the foregoing table (page 166). Age exerts a two-fold influence. Not only are young children bad subjects for diphtheria, but in them the disease shows a greater tendency to assume the laryngeal and nasal forms.

3. *Sex* has less influence. The mortality amongst males in the foregoing series was 26.0 per cent; whereas in females it was 23.6 per cent.

4. *State of health.*—Those who are subject to any wasting disease, or who are cachectic in virtue of ill-nutrition or a tuberculous dyscrasia are prone to severe attacks. So also are those who are actually suffering from other acute infectious disease, particularly measles, whooping-cough, and scarlet fever, as the malady then usually affects the respiratory passages. The mortality of co-existent measles and diphtheria in pre-antitoxin days was over 80 per cent.

5. *Length of time before coming under treatment.*—The importance of early treatment has always been recognised in respect to local remedies, but it assumes a paramount importance in the case of treatment by antitoxin. A procrastination of twenty-four hours in one's determination to give antitoxin may make just the difference between life and death in a young child. In laryngeal attacks the

necessity for tracheotomy is often averted, and in faucial cases its importance is nearly as great.

Bacteriology and pathology. — The specific contagium of diphtheria, the Klebs-Löffler bacillus, is always present in the exudation, and in the superficial layers of the affected mucous membrane. Its local multiplication is attended with the formation of a specific toxin, which is absorbed into the circulation, and, by its noxious effects on certain tissues, is productive of the particular symptoms of the disease. Diphtheria, then, like tetanus, is an intoxicative rather than a truly infective disease, in which the blood becomes infested with the micro-organisms themselves. Recent research, however, has shown that this limitation of the bacilli to the local lesion is not absolute; for in severe attacks they have been found, not only in the subjacent lymphatic glands, but in the tissue of the lungs, the spleen, and more rarely the kidneys. The fact is, nevertheless, beyond dispute that diphtheria is primarily, if not essentially, a local infection. The toxin of a virulent culture of the bacillus proves lethal to rabbits and guinea pigs injected with it, and tissue changes are produced in them similar to those found in fatal cases of human diphtheria. As to its chemical nature, it has been variously held to be an enzyme, a toxalbumin, and an albumose.

The Klebs-Löffler bacillus is polymorphic and varies in length from 2 to 6 μ. It is not motile and does not form spores. It is frequently somewhat curved, though more often straight, and commonly shows a slight swelling of one or both ends (Plate I.). It stains irregularly, and consequently often presents a beaded appearance, or looks as if segmented. When alkaline methylene blue is used, the irregularity of the staining is most apparent; so much so that a dark dot may usually be observed at each pole of the bacillus, an appearance which is often well brought out by Gramm's method. This effect is commonly more pronounced in bacilli taken from a culture than in those removed directly from the throat. Two chief varieties of the bacillus are recognised, the long form and the short. The former is much more distinctive than the latter, the identification of which is sometimes very difficult. In old cultures there is a tendency for the bacilli to become club-shaped or pyriform, one end being much swollen, the other tapering off to a fine point. Clubbing, however, is sometimes seen in newly-formed colonies. Although considerable variation may be noted in respect to the form and size of individual bacilli, their mutual arrangement in the microscopic field is often very characteristic, being frequently aggregated into small clusters, some of the members

of which lie parallel to each other, whilst others are disposed at various angles; the general appearance of the group thus resembling that of a Chinese alphabetical character.

The colonies grow on blood-serum at 37° C., can be recognised by the naked eye in twelve to sixteen hours as slightly raised, round, grayish-white dots, and at the end of twenty-four hours are usually as large as a fair-sized pin's head. On glycerine-agar at the same temperature they grow somewhat less rapidly, and the colonies are slightly grayer and more translucent at their periphery than in the centre. On nutrient gelatine at room temperatures, the growth, though far slower, is more characteristic. The colonies tend to become faintly yellow in tint, their centres raised, and surrounded by concentric rings, which give them a ripple-like appearance, though this is not very obvious until after a week or ten days' growth. No liquefaction of the gelatine takes place. When the bacillus is grown in broth the medium soon becomes turbid, and deposits a white chalky sediment on the bottom and sides of the tube.

Bacilli are frequently found in the throat, either alone or in association with the true diphtheria bacillus, which, both morphologically and in their cultural behaviour, are indistinguishable from it, but differ in that they are quite devoid of virulence. Apart from any difficulty in respect to the identification of these *pseudo-diphtheritic* bacilli, there is considerable difference of opinion amongst bacteriologists as to whether they are true diphtheria bacilli which have become attenuated, or whether they should be more properly regarded as members of an entirely distinct species. This point is by no means conclusively settled. The local reaction resulting from the multiplication of the bacillus of diphtheria on the surface of a mucous membrane constitutes the lesion which is so distinctive of the disease. It is essentially an inflammation, characterised by hyperæmia, stasis, the accumulation of leucocytes, proliferation, followed by necrosis, of the epithelial cells, and the exudation between them, and on their surface, of more or less fibrin. This either takes the form of a thin, loosely-coherent pellicle, or, should the epithelial layers be involved to a greater depth, of a thick tenacious membrane, in which distinct evidence of lamination can be made out. In diphtheritic croup membrane is found lining the trachea and bronchial tubes, in severe cases, even to their smallest ramifications, where it becomes lost in a layer of muco-pus. More or less broncho-pneumonia is always present, usually of a truly diphtheritic nature, the alveoli being stuffed with

fibrin, leucocytes, and bacilli; or it may be of a septic order, due to pyococcal infection. The common pyogenetic and putrefactive organisms may be detected in the surface of the exudation in practically all cases of diphtheria; but in some instances a definite septic invasion takes place. These cases of "mixed infection" are almost invariably severe.

Post-mortem appearances.—The appearances yielded by the organs in fatal diphtheria are not very distinctive. In severe faucial cases the spleen is often somewhat enlarged, and the same is true of the kidneys, of which the cortex is broader and paler than normal, while the epithelial cells lining the tubules usually show considerable fatty change. The heart muscle is pale, and its component fibres to a variable extent will be found to have undergone fatty or granular degeneration, particularly, though not necessarily, in cases fatal through sudden cardiac failure. The change may be well marked as early as the fourth or fifth day of the disease. The cardiac cavities, especially the left ventricle, are often markedly dilated. It is on nerve tissue, however, that the most distinctive effects of the diphtherial poison are seen. Irregular foci of acute parenchymatous degeneration are found scattered haphazard throughout the peripheral nerves, and, in less characteristic degree, in the sympathetic. The change affects certain fibres alone in a particular nerve, the others being spared; and since in a mixed nerve separate fibres to muscles, and points in the skin to which the degenerated fibres run are alone affected, not only does paresis of the muscle, rather than paralysis, result, but the distribution of the wasting and anæsthesia is necessarily irregular.

The **differential diagnosis** between diphtheria and certain cases of non-specific inflammation of the faucial, nasal, and laryngeal passages which simulate it is often extremely difficult, especially in respect to follicular tonsillitis. It practically resolves itself at the present day into whether or not the Klebs-Löffler bacillus can be detected in the exudation or discharges. The test, however, valuable though it is, is unfortunately not infallible. In most cases bacilli disappear in three or four weeks, but they may persist for several months after the throat has recovered, and are even occasionally found in the fauces and nasal discharge of perfectly healthy persons, especially those who have been in attendance on patients suffering from the disease. Although, for this reason, it is impracticable to strictly regulate the duration of a patient's isolation by the fact of the presence or absence of the bacillus, its

value as evidence as to the specific character of an inflamed throat cannot be denied.

Treatment.—Although nothing can compare with the injection of antitoxic serum in the treatment of diphtheria, representing, as it does, a true specific for the disease, the simultaneous adoption of efficient local treatment should not be omitted. This is best effected by syringing out the pharynx, and, if necessary, the nasal passages, every two, three, or four hours with some antiseptic and astringent solution in the manner described in the treatment of septic attacks of scarlet fever. By this means the local multiplication of the diphtheria bacillus, and other micro-organisms, is to some extent inhibited, and offensive secretions are cleared away. A solution of chlorine, or one of formalin (1 in 200), or chinosol (1 in 600) is the best. The throat may be sprayed occasionally with a weak solution of sulphurous acid, and one of borax and bicarbonate of soda (of each 10 grains to the ounce) is sometimes useful. Neither gargling or swabbing out the fauces are of much practical value, and the same thing is true of the local application of powdered sulphur, which used to be widely practised.

In early laryngeal obstruction a steam tent is indicated. For its relief intubation is often successful in the hands of a skilled operator. Tracheotomy, however, is preferable in most cases.

In cardiac failure drugs are of little value, but the hypodermic injection of liquor strychninæ (2 to 5 m.) every four hours, and frequent small doses of alcohol should be tried.

A dose of from 2000 to 8000 units of antitoxin, according to the severity of the attack, should be given at the earliest possible moment in every case when the patient is a young child. In the mild form of attack in adults it may be withheld, but the case must then be carefully watched. No regard need be paid to the age of the patient in regulating the dosage. Should there be even the faintest suggestion of croup, a full dose of 8000 units should be given at once, as the necessity for tracheotomy will probably be thereby averted. In all but the mildest attacks a half dose should be repeated at least every twenty-four hours until the exudation has definitely commenced to separate. It is of paramount importance that *the treatment should be commenced early*. The serum can be of no use after the tissues have been irreparably damaged by the toxin already absorbed. The injection is preferably made under the skin of the back or loins, with careful previous sterilisation of the syringe and its needle. Under the influence of early treatment with antitoxin, the development of the disease is checked, the faucial

swelling and rhinorrhœa abate, and the membrane separates earlier, with the result that the patient's distress is greatly lessened, laryngeal obstruction seldom supervenes, and the mortality is greatly reduced, especially amongst the tracheotomy cases. The fact that a rash, usually of a measly, or urticarial character, or a short period of irregular pyrexia, or, though far more rarely, some pains in the joints may arise a week or ten days after the antitoxin has been given, is no reason against its employment, as they are never attended with any permanent ill effect.

F. Foord Caiger.

EPIDEMIC PNEUMONIA

The clinical features of croupous pneumonia, especially its sudden onset, its definite course, and termination in a crisis, give it a striking resemblance to such specific febrile diseases as typhus fever or smallpox. Nor do the occasional occurrence of true relapses diminish the resemblance. The apparent absence of infectiveness in the vast majority of instances does not necessitate its exclusion from the list of specific febrile diseases, as such maladies present every degree of infectivity, the amount of this property being determined in part by the accessibility of the infective material to the surface of the body and in part by the environmental conditions. The influence of environment is probably at its minimum in anthrax and smallpox. It is very great in rheumatic fever and in pneumonia, in which auxiliary factors are required besides the "unconditioned microbe" to complete the causation of the disease. The regular seasonal exacerbation of the disease (March to May), and the fact that in certain years it is prevalent in such excessive amount as to deserve the name of "epidemic," confirm the same view. The official figures of the English Registrar-General, however, do not lend themselves to a demonstration of the notion that in certain years croupous pneumonia is epidemic; because in them all forms of pneumonia are necessarily reckoned together. Even if an attempt were made to separate them, without universal autopsies by skilled pathologists the results would require to be accepted with caution. The following figures, contributed by MM. Montané and Duponchel to the French Comité de Santé, are less open to objec-

tion. They give the morbidity rate from pneumonia in the 50th line regiment of Périgueux among an adult population remaining fairly constant throughout the period. The corresponding rates for typhoid fever are given for comparison :—

	Pneumonia.	Typhoid Fever.		Pneumonia.	Typhoid Fever.
1878	.83 per 100	.00 per 100	1885	.50 per 106	1.36 per 180
1879	.36 ,,	.28 ,,	1886	1.13 ,,	2.25 ,,
1880	.57 ,,	.42 ,,	1887	2.16 ,,	1.85 ,,
1881	.00 ,,	.00 ,,	1888	3.32 ,,	.52 ,,
1882	.45 ,,	.35 ,,	1889	3.37 ,,	.52 ,,
1883	.00 ,,	4.32 ,,	1890	.73 ,,	.36 ,,
1884	.40 ,,	1.53 per 180	1891	1.85 ,,	.16 ,,

Thus the sickness rate from pneumonia was irregular until 1883, then increased regularly until 1889, when the epidemic culminated, subsequently declining.

It may be argued that variations like the above may be caused merely by climatic causes, such as excessively cold winters. The facts do not confirm this view ; and it may be added that the favouring influence of climatic influences does not exclude the operation of a specific micro-organism, which, although it cannot "unconditioned" cause pneumonia, is so far the essential cause that the disease does not arise in its absence. Bacteriology, moreover, shows the presence of micro-organisms in pneumonia (see Vol. IV.).

It may be that there is more than one disease under the name croupous pneumonia, and that this may explain the difference between sporadic cases, which nearly always occur singly, and epidemic cases, occurring in small groups or in large epidemics. The relationship between sporadic and epidemic pneumonia may resemble that between an ordinary febrile catarrh and influenza, or between summer diarrhœa and cholera, or between catarrhal jaundice and acute yellow atrophy of the liver. It may, on the other hand, more closely resemble that between ordinary ague and the pandemic ague, which has devastated continents in the past, or between sporadic and epidemic cerebro-spinal meningitis. Cerebro-spinal meningitis becomes epidemic under extremely insanitary local conditions. There is evidence of the same kind for pneumonia. This is well instanced by an outbreak occurring in 1883 at La Salpêtrière. In the early part of the year the sewers of this establishment were in process of reconstruction and deep trenches dug, the work being executed in succession in three chief courts or yards. The work was watched by a number of hysterical and epileptic patients, and each portion of the work as it was begun was followed by a new case of pneumonia. Four women

altogether were attacked, those who had not been outside close to the trenches escaping. In 1874 Drs. Grimshaw and Moore noted an increase of pneumonia in Dublin, during a prolonged drought, which they attributed to diminished flushing of the sewers. A serious epidemic of pneumonia raged in Florence in the winter of 1877-78, which was ascribed by Bauti to foci of telluric infection, especially to the stagnation of the River Arno, owing to the prolonged drought of the preceding May to October.

It would appear also that foci of the disease may exist in dwellings. Thus Mendelsohn ("Die Infect. Nat. der. Pneum.," *Ztschr. f. klin. Med.* 1884, t. vii. p. 191) gives the instance of a coachman who went to lodge on the 3rd of April 1883 in a very dirty house, the first few days of his stay there being occupied in cleansing and sweeping. On the 20th April his wife fell ill with pneumonia, next day a child of five years old, a day later the baby, aged fifteen months; the third child, aged three years, escaped. On the 26th April the coachman himself began with the same disease. He was removed to the hospital, returning to the same lodging convalescent at the end of May, whence he had to return to hospital in June with a second attack of pneumonia. It would be easy, did space permit, to give numerous instances of epidemic pneumonia in connection with prisons and barracks.

The evidence of direct contagion is feeble. It would appear to be exceptional; but Netter ("Contagion de la pneumonia," *Arch. gén. de méd.* 1888, 7^{e} serie, t. xxi. p. 530) has collected a number of scattered observations. The following case, reported by Schrœter, may be instanced. A man aged twenty-four years had an attack of rheumatism in October 1887. After six weeks, when he was convalescent, his father was brought to the house with left-sided pneumonia, and occupied the same bed as the son. On the eighth day of the pneumonic attack, the son, who had not hitherto left his room, began with typical right-sided pneumonia. Wynter Blyth has narrated the case of a young woman who contracted pneumonia while nursing her father for this disease, and who, after she had been taken to her own home, communicated the same disease to her husband. The following case is interesting, as the infection appears to have clung to fomites (*Lyon méd.*, 28th Avril 1889). A butcher's child was convalescing from pneumonia, and about this time the butcher's servant boy began with pneumonia (10th December). He was removed to the hospital, and on the 15th December a second boy took his place, sleeping on the same bed and in the same clothes. Two days later he was seized with pneumonia. A third

boy arrived on the 18th December; he slept with the second boy for two nights, and thirty hours later began with pneumonia.

The preceding observations raise a strong presumptive case for the contagiousness of pneumonia, under exceptionally insanitary conditions of soil or dwelling. It is not likely that the multiple cases are explicable merely as coincidences.

Outbreaks of pneumonia have occurred in this country at Middlesborough (682 cases and 143 deaths) and at Scotter. In the former outbreak Klein was unable to discover either the micrococcus of Friedlander or the diplococcus of Fränkel and Weichselbaum, but found instead a distinctive bacillus. This observation, among others, renders it likely that in croupous pneumonia we have to deal with several diseases, not yet differentiated. This fact, if confirmed, may explain the varying infectivity of the disease. One circumstance has to be borne in mind in connection with epidemics of pneumonia. Some of them have coincided in time with the prevalence of epidemic influenza. It may be, therefore, that the pneumonia was but a local complication of this disease. This explanation only, however, accounts for a small proportion of the recorded epidemics of pneumonia.

Historically there are numerous accounts of epidemic pneumonia. Some of these have spread over wide tracts of country, as for instance those of 1564 in Italy, Switzerland, and Western Germany, of 1779 in Italy, of 1783-85 in France, of 1863-75 in the United States, and of 1857 in Bolivia, Peru, and Western Brazil (Hirsch). We still lack, however, accounts of true epidemics of pneumonia in which careful autopsies have been made of fatal cases, and in which the exact cause of the infection has been traced and described.

The clinical characters of the disease will be treated of elsewhere.

ARTHUR NEWSHOLME.

INFECTIVE MENINGITIS

The pia-arachnoid membranes are not infrequently the seat of inflammation consequent upon the invasion of several distinct micro-organisms. Associated with the different varieties of causal virus there is some difference in the clinical course and symptoms of the resulting affections. The various forms at present recognised are as follows :—

1. Epidemic cerebro-spinal meningitis. 2. Posterior basic meningitis. 3. Suppurative meningitis. 4. Tuberculous meningitis.

In the first and second forms, and also in the third, when the disease is not secondary to pneumonia, erysipelas, middle ear disease or injury, as it usually is, the anatomical lesions found post-mortem are almost entirely confined to the meninges, and the symptoms presented by the patient are as entirely referable to the meningeal inflammation. For these reasons these maladies will be described here; the tuberculous variety, as well as the meningitis associated with syphilis and new growths, will be treated of elsewhere.

Epidemic Cerebro-spinal Meningitis

Syn. Cerebro-spinal Fever—Spotted Fever—Cerebral Typhus

An acute febrile disorder characterised by symptoms indicative of special affection of the central nervous system, and very frequently accompanied by a rash.

Since 1805 numerous epidemics on the Continent of Europe, in Ireland, and in North America have been recorded. Great Britain has been free from large outbreaks, though minor ones have not been rare, and sporadic cases not at all infrequent. The malady is most prevalent in temperate latitudes, but it also occurs in sub-tropical climates. On *à priori* grounds it might be expected to have a universal distribution, a view which receives confirmation from its occurrence in India, and from the record of a few cases in Australasia and the Fiji islands.

The epidemics have occurred mostly in winter and spring, and among the predisposing causes may be enumerated ill or insufficient nourishment, exhaustion, over-crowding, and unwholesome sur-

roundings. Notwithstanding the frequently recorded epidemics among persons closely associated, such as are found in gaols, schools, workhouses, asylums, and barracks, direct contagion is slight or negative, and the exact method of communication is at present undetermined. It is probably due to this circumstance that comparatively few individuals are attacked in any epidemic.

While children and young adults are especially liable, no age is exempt, and though robust males in the prime of life are frequently attacked, yet after thirty-five years of age the liability is slight. The disease has been known to be transmitted from the mother to the fœtus *in utero*, as shown by identical post-mortem appearances in both.

After an **incubation period** of unknown though probably short duration, during which there may be vague or ill-pronounced premonitory symptoms, the disease declares itself with remarkable suddenness, the principal initial **symptoms** being intense occipital headache, shivering, and vomiting. These symptoms, accompanied by prostration, rapidly increase in intensity; the patient tosses restlessly about, frequently becoming delirious; the face is drawn and pale; an herpetic eruption appears on the face, and purpuric spots on the legs and elsewhere. The skin is extremely sensitive. The head is often retracted, and there is pain and tenderness in the back and limbs, frequently severe. The pupils are small, the conjunctivæ injected, and frequently there is strabismus and sometimes ptosis and facial spasms. The condition of the tongue is variable, though in severe cases it is much furred. The abdomen is retracted and the bowels constipated. By the third or fourth day the pulse and respiration increase in frequency, the temperature ranging from 100° to 104°. The decubitus is lateral, with the legs drawn up. The vomiting continues. The prostration and the spasm of the muscles of the neck and back increase in severity. There is retention or incontinence of urine, and the patient, who has been gradually becoming deaf and drowsy with sighing respiration, lapses into unconsciousness, and dies from pulmonary congestion and œdema.

Though the foregoing may be taken as the description of a severe case, it is necessary to point out that the disease presents more than one clinical picture. Four or five types are usually described—malignant, severe, mild, and abortive, and considerable variety of symptoms characterises different epidemics.

In the *malignant form* the patient may die in a comparatively few hours in a condition of collapse and coma. It is in these cases that petechiæ and purpuric blotches are so well marked and of such fatal

significance. In the milder forms all the symptoms are less violent, and some, such as the petechiæ, are absent. The *abortive type* is usually recognised by the presence of headache, and some malaise occurring during an epidemic. To these may be added the *intermittent variety*, in which remissions and exacerbations of the symptoms occur, and the *typhoid*, wherein muttering delirium, dry, brown-furred tongue, and other typhoid symptoms are prominent phenomena.

Several symptoms and **complications**, some of which have important **sequelæ**, require to be specially noticed. Herpes of the face and lips is present in the majority of cases, and may occur also on other parts of the body. Though herpes is the most common, urticaria, pemphigoid bullæ, and erythematous roseolar eruptions are also described. In the severe and malignant types the skin is the seat of hæmorrhagic petechiæ and blotches, and these may be so extensive and prominent as to warrant the term cutaneous hæmorrhages. Of late years, however, less note has been taken of rashes or eruptions, with the exception of herpes. Coryza is occasionally present, manifesting itself either before the outbreak or during the attack. The chief interest of this symptom is that the nasal and faucial mucosæ may possibly be the portals of entry of the virus.

Of late attention has been drawn to Kernig's sign, by which is meant the reflex contraction of the flexor muscles which occurs when an attempt is made to extend the leg on the thigh, as indicative of meningitis. To elicit this phenomenon the patient must be placed in the sitting posture. The condition of the reflexes is variable, that is, they may be normal, exaggerated, or absent.

The temperature mostly ranges between 100° and 104°, though in some cases, usually rapidly fatal, it may rise but little or not at all; while on the other hand it may ascend as high as 107°. There is no special curve or type, and all that can be said is that it is irregularly remittent.

The pulse is sometimes rapid, 100-120°, at any rate in children, for in adults it may be quite slow, and quite out of relation to the temperature. There is little to be said about the respiration, except that it may be laboured and sighing; still, pulmonary complications must always be remembered.

One of the most frequent issues is eye trouble, such as palsy of the ocular muscles, and conjunctivitis, which may become ulcerative. Blindness has not infrequently resulted from suppuration of the internal parts of the eye. Disease of the ear, resulting in permanent deafness or deaf-mutism in young children, is not at all

uncommon, and is decidedly more frequent than in posterior basic meningitis. This sequela is due to direct extension of the inflammation from the meninges to the labyrinth, and also to the affection of the tympanum. Besides the eye and ear, the special senses of taste and smell may also become impaired.

Other less constant and less common features are the presence of albumen in the urine, hæmaturia, optic neuritis, and, in children, convulsions.

Perhaps the most important sequela is chronic hydrocephalus. This usually manifests itself during convalescence; but its presence may be suspected if the vomiting be protracted, and especially if there be unaccountable rises of temperature and the headache be persistent.

Other complications and sequelæ which may be met with are, suppurative and non-suppurative arthritis and periarthritis, pneumonia, broncho-pneumonia, pleurisy, peri- and endo-carditis, and palsy of the limbs. The paralysis of the extremities may be hemiplegic, paraplegic, or monoplegic in distribution. If monoplegic, the arm is the part most frequently affected.

Emaciation is a distinct feature of the disease; sometimes it is extremely marked and then is often associated with severe damage to the central nervous system.

The principal and indeed the only essential **morbid appearance** is a suppurative or fibrino-purulent leptomeningitis of the brain and cord. The distribution of the exudation in the brain is irregular, and affects both vertex and base. In amount and extent it is extremely variable; it may be considerable even in rapidly fatal cases, though under these latter circumstances mere hyperæmia only may be visible to the naked eye. In the spinal cord the exudation is most marked on the posterior aspect and towards the lower end. The cerebral ventricles are usually distended with turbid fluid, and the lining membrane disintegrated. Though the spleen may be much enlarged it is frequently but little or not at all increased in size. Micro-sections show that the subarachnoid exudation is principally cellular, and chiefly leucocytic, and the presence of micro-organisms in the exudate has been demonstrated.

In addition to the essential features there are often, as already intimated, pneumonia, broncho-pneumonia, pleurisy, peri-, and endo-carditis.

Special methods of investigation (*e.g.* Nissl's and Marchi's) have determined the existence of degenerative changes in the nerve cells

and fibres of the central nervous system. The cells may be swollen, granular, their shape disfigured and their chromatic bodies absent (chromatolysis). The nucleus may be displaced or even lost.

Bacteriology.—The microbe to which the disease is due is the *diplococcus intracellularis meningitidis* (Weichselbaum). This organism has been discovered not only in the exudation, examined post-mortem, but has also been obtained from the spinal fluid withdrawn by lumbar puncture during life.

The diplococcus is very small, and occurs most often in groups inside the cells of the exudation. Here and in cultures it is frequently grouped in pairs, and for this reason has been described by some observers as a tetracoccus. It stains with the ordinary aniline dyes, but does not stain by Gram's method. One of its characteristics, as described by Weichselbaum, is its very brief vitality, a point in which it differs from the diplococcus of posterior basic meningitis. There are other slight differences both on culture and on inoculation between these two micro-organisms, but it is probable that they are closely related.

From the pneumococcus the diplococcus intracellularis differs in many respects, morphologically, in culture and on inoculation. The diplococcus intracellularis is found not only in the epidemic, but also in the sporadic cases of this disease. Some cases, however, which would in the past have been included under this head, are now known to be due, some to the diplococcus of posterior basic meningitis, some to the pneumococcus, which until recently was regarded as responsible for the malady now under consideration.

Whether the pneumococcus does give rise to an epidemic form of meningitis is uncertain; but there are certain relationships apparently existing between pneumonia and the epidemic cerebrospinal form of meningeal inflammation which are striking, such are the same seasonal prevalence and frequent coexistence of the two diseases, especially in crowded gaols and barracks, the sudden onset and marked liability to the appearance of herpes.

Prognosis.—The mortality in this disease, especially in some epidemics, is high, and has ranged from 20 to 80 per cent, so that the average mortality may be assumed to be about 50 per cent. In the more malignant cases death may take place in a few hours to a few days (1-8). As a rule, convalescence is tardy. Mild cases may get well in a week or two, while others, where the symptoms have been only moderately severe, may last for five or six weeks or longer. It is advisable to wait for ten to fourteen days

after the symptoms have subsided before stating that the patient is to be regarded as safe.

Apart from special complications, such as hydrocephalus, otitis, endocarditis, and pneumonia, there is always grave danger from asthenia and marasmus, conditions which may follow mild as well as severe cases. When these conditions are marked the patient, after lingering for months, usually dies from toxæmic cachexia. The prognosis must depend chiefly on the severity of the symptoms, though some assistance may be derived from the character of the epidemic and the time it has lasted, for the cases are usually more severe at the beginning than at the end of the outbreak. When the initial symptoms are severe, when coma supervenes, when hæmorrhagic blotches, especially if extensive, make their appearance, the prognosis is extremely grave.

The **diagnosis** will depend in the first place on the recognition of the more striking and salient symptoms, namely, headache, vomiting, fever, pain in the back, retraction of the head and the presence of herpes. Few disorders have such a sudden onset, and are accompanied from the first by so much prostration. A positive and early diagnosis might therefore seem a simple matter. Yet, owing to the presence of headache, of constipation, and of the absence of spots, enteric fever has been mistaken for cerebro-spinal meningitis. With typhus fever it might more easily be confounded owing to the presence of a petechial rash and of prostration. The rash, however, appears more suddenly than that of typhus, from which it is further distinguished by the greater intensity of the nervous symptoms. Purpura hæmorrhagica and hæmorrhagic variola have both been confused with this disease. From tuberculous meningitis it is distinguished by the gradual onset, the less severe symptoms and the absence of rash in the latter; from suppurative meningitis, by the absence of some obvious exciting cause, such as traumatism or disease of the ear; from influenza, when severe, and when there is fever, headache, pain in the back and prostration, by the absence of vomiting, of any marked affection of the cranial nerves and retraction of the head.

Heart or lung complications, especially if early, might cause a difficulty in coming to a conclusion, for the occurrence of cerebro-spinal symptoms might lead to the suspicion that the affection of the central nervous system was secondary and metastatic.

As may have been inferred from a consideration of the morbid appearances, the line of **treatment** must be symptomatic and palliative, and in a great measure expectant. Still there is a consensus of opinion in favour of giving opium, or what seems to

answer better, morphia, by hypodermic injection, in order to allay the general irritability, to soothe the pain, to promote sleep, and in some degree to restrain vomiting.

The abstraction of cerebro-spinal fluid by lumbar puncture has been practised not unfrequently of later years, and cases of cerebro-spinal meningitis are reported wherein this procedure has been followed by recovery. Though, owing to the general character of the disease and the parts principally affected, too much must not be expected from the removal of cerebro-spinal fluid, the results from lessening the tension are sufficiently encouraging to warrant its adoption in this form of meningitis.

Subcutaneous injections of Liq. hydrarg. perchlor. have been strongly advocated, improvements following, it is said, the second or third injection.

The headache and spinal pain are sometimes alleviated by the use of ice-bags, while blisters have been found unsatisfactory, and their use is to be deprecated.

The results from general abstraction of blood are not encouraging, though local depletion by means of leeches may possibly be found to afford some relief.

To check the vomiting, hydrocyanic acid with bicarbonate of soda in simple draught or in effervescing mixture may be tried, alone or in combination with one of the bromides as a sedative. Though the foregoing and other drugs are sufficiently approved for restraining retching and vomiting, their exhibition will depend on the tolerance of the stomach to interference, and it may be found advisable to adopt a cold liquid and scanty dietary until the main symptoms are subsiding.

Constipation should be treated by enemata until convalescence has set in and the alimentary canal is in a condition to bear aperients.

During convalescence, which is frequently protracted and accompanied by general debility and emaciation, headache is not uncommon, and sometimes severe; for this antipyrin or chloral and bromides are indicated; while as a general tonic a mixture of quinine and iodides should be administered.

R. G. Hebb.

Posterior Basic Meningitis

The recognition of posterior basic meningitis as a specific disease is of quite recent date. It had been observed for many years that there occurred, chiefly in infants, a disease characterised by prolonged and extreme retraction of the head, and it was with reference to this striking symptom that the description of the disease by Dr. Gee and Dr. Barlow in a paper on "The Cervical Opisthotonos of Infants" appeared in 1878. It was not, however, until Dr. Carr in 1897, and shortly afterwards Dr. Barlow and Dr. Lees, drew attention to the constancy of the symptoms, and the general likeness to a specific disease, that its true position was recognised, and its infective nature was finally confirmed by the discovery of the micro-organism to which it is due.

The exact relationship of this disease to that known as "Epidemic Cerebro-spinal Meningitis" has not yet been fully ascertained, for although the bacteriological evidence shows them to be very closely related, if not identical, there are slight differences in the bacteriology, and more particularly in the clinical aspect of the two conditions, which make it perhaps desirable, at any rate for the present, to consider them separately.

Etiology.—Posterior basic meningitis, though it sometimes occurs in later childhood, is most common during the first year of life, and seldom occurs after the end of the second year. It is frequently seen during the first six months of life, a period at which tuberculous and epidemic cerebro-spinal meningitis are quite uncommon. Girls and boys are affected with about equal frequency. The disease shows a very marked seasonal variation; it is much commoner in winter and spring than in summer: fully two-thirds of the cases have their onset between the beginning of January and the end of May.

It would appear to be endemic in most large towns and cities, and cases have been observed both on the Continent and in America, so that although it is impossible yet to say anything definite as to its geographical distribution, there can be little doubt that it is a widely-spread disease, and is by no means limited to the British Isles.

In spite of the infective character of the disease no evidence whatever of transmission from infant to infant has yet been observed. The close resemblance to the sporadic cases of so-called epidemic cerebro-spinal meningitis must, however, be borne in mind, for it is at least possible that the posterior basic disease of infants is only one sporadic manifestation of the epidemic disease.

In some cases a history of a fall or blow preceding the onset of the illness is obtained; in others some slight catarrhal symptoms, a cough or "a cold" have occurred, but it seems very doubtful whether these bear any causal relation to the disease.

Bacteriology.—The immediate cause of the meningitis is an infection of the brain with a specific micro-organism, the diplococcus of posterior basic meningitis, which shows only very slight differences from the diplococcus intracellularis of epidemic cerebro-spinal meningitis. It must not be confused with the pneumococcus, from which it differs widely, and from which it can easily be distinguished by culture and by inoculation. The diplococcus is very small; its average length, measured in the meningeal exudation, is 1.2 μ to 1.5 μ. The two cocci of which it consists have their opposed surfaces more or less flattened, and are separated by a narrow clear space. It shows a marked tendency, especially in cultures, to grouping in pairs side by side, so that an appearance like that of a tetracoccus is produced. It is ærobic, and is easily cultivated at a temperature of about 37° C. Its vitality is greater than that of the pneumococcus or of the diplococcus intracellularis, while its virulence on inoculation seems to be less.

The diplococci are found both free and in the cells of the exudation, and in the cerebro-spinal fluid, during the acute stage of the disease, but they disappear usually after a few weeks as the inflammation subsides.

It is probable that, as in other forms of meningitis, a mixed infection may occasionally occur, other micro-organisms gaining access to the meninges either at the same time with the specific micro-organism or at a later period; but such an occurrence would seem to be extremely rare.

The channel of infection in this disease has not yet been ascertained. There is no evidence to show that infection occurs through the ear.

Symptoms.—The onset of the disease is sudden: an apparently healthy infant is seized with vomiting, becomes feverish, and perhaps screams without apparent cause. Convulsions may occur at this stage, but more commonly begin later.

Within a few hours, or at most within a few days, of the onset the head is noticed to be drawn back; sometimes indeed this is the first symptom noticed. Of all the symptoms of posterior basic meningitis the head retraction is by far the most constant and the most characteristic. It appears very early in the disease, and lasts usually for several weeks or even months. The retraction varies in

degree in different cases, and may vary from day to day; it may be so slight as to be only just noticeable, but in the majority of cases is quite obvious, and in some is so extreme that the occiput almost touches the buttocks. Where this happens there is extreme opisthotonos of the dorsal spine as well as of the cervical; more often, however, the opisthotonos is limited to the cervical region, the head being thrown backwards, so that there is barely room for two fingers between the occiput and the upper dorsal spine, while the dorsal spine itself is rather in a position of kyphosis.

Clonic convulsions may occur at any period of the disease, but they are not a marked feature, and are sometimes absent throughout. A commoner condition is one of tonic rigidity, and as the disease becomes advanced the infant often lies on its side with head thrown back and limbs rigidly extended, the forearms at the same time being fully pronated, so that the palms of the clenched hands look outwards, while the shoulders are drawn back, and the legs tend to cross owing to some adductor spasm of the thighs.

Champing movements of the jaw and grinding of the teeth are curiously common in this disease, although not peculiar to it; either of them may continue sometimes for hours.

With the head retraction there is often a staring appearance of the eyes, due apparently to a spasmodic raising of the upper lid, so that the palpebral fissure is widely open; and this staring appearance becomes even more noticeable when there is added to it the vacant look of blindness.

Blindness is present in about one-third of the cases of posterior basic meningitis, and appears to be quite independent of any gross changes in the eye: there can be little doubt that it is entirely central in origin. In most cases, even with complete blindness, there is no optic neuritis, and in the rare cases where inflammatory changes are present in the disc they are usually very slight. Paralysis of the ocular muscles is seldom a marked symptom; in nearly half the cases strabismus is absent altogether, and when present it is often slight and transitory; paralysis of other cranial nerves is extremely rare. Slight nystagmus is not uncommon. Deafness has occurred in a few cases, but is quite exceptional.

Sensation appears to be normal; there is evident pain when any attempt is made to push the head forward into its natural position, but otherwise the infant lies quietly on its side, apparently free from pain, and only giving a sudden start when disturbed.

The superficial reflexes are unaltered; the tendon jerks, especially the knee jerks, are usually over-active, especially in the

chronic stage of the disease, when there is sometimes ankle-clonus. The "tache cérébrale" is a less marked feature in this disease than in tuberculous meningitis.

Vomiting is one of the most constant of the early symptoms, and is usually more or less persistent throughout the disease. The bowels show less tendency to costiveness than in tuberculous meningitis, and diarrhœa is a common complication, especially towards the end of the illness. The urine shows nothing abnormal.

The pulse is usually more rapid than normal throughout, and if irregularity occurs it is slight and transitory; the marked slowness and irregularity of the pulse which occurs in tuberculous meningitis is not observed at any period of the posterior basic disease.

The respiration, especially in the later stage, frequently shows some periodic irregularity, long pauses alternating with a series of rather rapid respirations, but without the rhythmic increase and decrease in depth which characterises the Cheyne-Stokes' type of breathing.

The temperature at the onset is raised to 102° or 103°, and there is irregular pyrexia usually for the first two or three weeks. The temperature then gradually falls, and may remain normal for the rest of the illness, or may become subnormal where there is much vomiting and exhaustion. Sudden hyperpyrexia may occur just before death. In some cases, and these usually the more severe, there is persistent and considerable pyrexia of a remittent or intermittent type throughout the illness.

In most cases where the disease is prolonged beyond a few weeks wasting is a marked feature; the emaciation may be extreme.

Rashes, especially the herpes and purpura, which are so common in the epidemic form of meningitis, are almost invariably absent in the posterior basic disease of infants, but too much stress must not be laid on this as a distinguishing feature, for very rarely a labial herpes has occurred at the onset, and at a later period a generalised blotchy erythema has been seen.

Complications.— The most important, because the most frequent, and the most fatal is *hydrocephalus*. In most cases where the disease lasts longer than a few weeks the head is noticed to be increasing in size, the fontanelle becomes bulged, and the eyes are turned downwards by increasing intracranial pressure, and even where death occurs earlier, and the only symptom of hydrocephalus during life has been fulness of the fontanelle, there is generally found after death to be some dilatation of the ventricles, the almost inevitable

result of the adhesive inflammation between the medulla and cerebellum.

Another complication, which was observed four times in forty consecutive cases, is an inflammation about the joints, giving rise to swelling and dusky redness. The process appears to be more often a periarthritis than a true arthritis; the exudation occurs about the neighbouring tendon-sheaths outside the capsule of the joint. It has recently been shown that this periarthritis is produced by a local infection with the same diplococcus as that found in the meningeal exudation.

Other accidental complications, such as diarrhœa and broncho-pneumonia, are apt to occur towards the end of the illness, when emaciation and exhaustion are extreme. With these occasional exceptions the thoracic and abdominal viscera are singularly free from obvious disease.

Prognosis.—The prognosis in this disease is much more hopeful than in tuberculous or in suppurative meningitis, pneumococcal or otherwise. While it may be doubted whether recovery ever occurs in these latter forms of meningitis, there is no doubt that quite an appreciable proportion, probably quite 10 per cent, of the cases of posterior basic meningitis recover. There may be complete recovery, but often there remains some permanent damage to the brain, resulting in some cases in chronic stationary hydrocephalus, in others in idiocy or imbecility, with or without hydrocephalus.

It is noteworthy that in cases of recovery the blindness of posterior basic meningitis has disappeared completely after some months' duration. The periarthritis and arthritis also tend to recover spontaneously.

The disease in many cases proves fatal about five weeks after the onset, but often the fatal result does not occur until the end of the third or fourth month of the illness, and in some cases, as already mentioned, the symptoms slowly subside and the child recovers.

The prognosis in any individual case depends mainly on the age of the patient—the younger the child the less is the chance of recovery—and the severity of the symptoms; long-continued pyrexia, extreme head retraction and much rigidity of limbs are all bad signs; but the gravest of all symptoms is the rapid supervention of hydrocephalus. In cases that seem to have recovered except for the presence of hydrocephalus, prognosis must be guarded, for although the hydrocephalus may appear to be stationary, such cases are apt to die suddenly and quite unexpectedly.

Diagnosis.—The disease with which posterior basic meningitis is most likely to be confused is tuberculous meningitis. The most important point of distinction is the presence of head retraction. There is often some stiffness of the neck in tuberculous meningitis, but anything like the definite and often extreme head retraction which characterises the posterior basic disease is very rare in tuberculous, and indeed in any other form of meningitis. At the beginning the diagnosis may be difficult, but the earlier age, the more sudden onset, the screaming, the absence of irregularity of the pulse, and the absence of paralysis of cranial nerves are points in favour of posterior basic meningitis. Later on the much slower course, the persistence of vomiting, contrasting with its more intermittent character in the tuberculous disease, in which vomiting often occurs only at the beginning and at the end of the illness, the absence of slow and irregular pulse, and of optic neuritis, the presence of blindness, and above all the persistent head retraction, usually make the diagnosis easy. Signs of tuberculosis in other parts of the body would of course favour the diagnosis of tuberculous meningitis.

From suppurative meningitis, whether due, as most commonly happens, to the pneumococcus or to other micro-organisms, the posterior basic form can generally be distinguished clinically by the absence of a primary focus of infection. In suppurative meningitis an obvious source of infection is almost invariably present, by far the commonest in children being pneumonia or empyema, or it may be otitis media or some other infective disease, such as erysipelas; the presence of such a source, together with the far more rapid course of the disease, which seldom lasts more than a few days, and the absence of head retraction would point to suppurative meningitis. Between epidemic cerebro-spinal meningitis and posterior basic meningitis the clinical differences are but slight. The limitation of this particular group of symptoms almost to early infancy, the more chronic course, the absence of the rash, especially of the herpes which has characterised some epidemics, the greater prominence of the head retraction, the absence usually of deafness, of conjunctivitis, of hyperæsthesia, these are the clinical points which, together with the slight differences of bacteriology and morbid anatomy, have been thought to separate the posterior basic from the epidemic disease. Head retraction, it must be remembered, is not always a symptom of meningitis; reflex irritation, sometimes from ear disease, sometimes from the teeth, may cause distinct head retraction for several days; in infants also with pulmonary and other disease, associated with much

dyspnœa, the head is sometimes considerably retracted, probably for the better use of the extraordinary muscles of respiration.

Morbid anatomy.—The essential feature of the disease is an exudation of lymph in the pia-arachnoid at the base of the brain and on the spinal cord. The exudation extends forward usually to the optic chiasma and sometimes slightly along the Sylvian fissures, but there is very rarely any trace of it on the vertex, which appears quite normal except for some flattening of the convolutions from the fluid distension of the ventricles, which is almost always present.

The most constant site of the inflammation at the base is the reflection of the arachnoid between the medulla and cerebellum; it is the inflammation here which determines some of the clinical features of the disease, especially the occurrence of hydrocephalus from obstruction of the foramina of Majendie and of Luschka, first by inflammatory exudation, and later by adhesions. The head retraction also is probably due to the inflammation in this region, which acts as a direct stimulus to the upper cervical nerves, and so produces spasm of the muscles which they supply. But this is not the whole explanation of this symptom, for, as already pointed out, it occurs also with ear disease without meningitis; in such cases, and probably to some extent in posterior basic meningitis, it is to be regarded as a reflex phenomenon.

In cases where the illness has lasted three or four months, all lymph exudation has disappeared, leaving only thickening and adhesions of the pia-arachnoid.

An important feature in the morbid anatomy of posterior basic meningitis is the absence of any obvious source of infection. The rest of the body is healthy except for such accidental complications as may happen towards the end of any chronic disease. Herein, as already pointed out, it contrasts markedly with ordinary suppurative meningitis.

Treatment.—No drug can be said to have any special influence over this disease. It has been thought that occasionally mercury has had some beneficial effect; some of the cases that have recovered have been treated with mercury, and it is certainly worthy of trial either by inunction or by internal administration. Potassium iodide has also been recommended, and may possibly hasten absorption of the lymph exudation.

The application of ice to the head or the nape of the neck, with due precautions against collapse, seems to check the vomiting in some cases, and may have some beneficial influence on the inflammation. Counter-irritants, if used at all, must be used with the utmost

caution ; the risk of producing troublesome sores on the delicate skin of an infant is hardly compensated by the doubtful value of this method of treatment.

Persistent vomiting may be very difficult to check ; dilute hydrocyanic acid in minute doses, a quarter to half a minim for an infant of nine months, may be tried, but as a rule no drugs will check it. Nasal feeding, which sooner or later almost always becomes necessary, owing to the obstinate refusal to take nourishment, may have some beneficial effect on the vomiting.

Every effort must be made to maintain nutrition ; rectal feeding must be used if necessary, and the diet must be carefully planned. Cod-liver oil and malt are useful, especially during the slow process of recovery.

Recently operative treatment has been attempted, chiefly with a view to establishing drainage of the ventricles, and so preventing the tendency to progressive and fatal hydrocephalus. The results hitherto have been disappointing ; in most cases death has followed shortly after the operation, sometimes with sudden hyperpyrexia ; in at least one case, however, the operation has been successful.

Puncture of the membrana tympani on both sides is advisable in doubtful cases, where there is any suspicion that the symptoms may be reflex in origin or due to the secondary meningitis of ear disease.

The arthritis and periarthritis tend to disappear spontaneously ; they should be treated by simple warm applications.

G. F. Still.

Suppurative Meningitis

Suppurative meningitis, by which is meant a purulent exudation in the pia-arachnoid of the brain and spinal cord, occurs under two conditions—the first, and by far the commonest, as a complication of some other infective disease ; the second, very rare, as a primary disease. The advance of bacteriology has made it evident that many, perhaps most of the cases of supposed primary suppurative meningitis, should be regarded as sporadic instances of so-called epidemic cerebro-spinal meningitis, being due to the specific micro-organism of that disease, namely the diplococcus intracellularis. There still remain, however, rare cases in which an apparently primary infection is produced by other micro-organisms.

Some confusion has been introduced into this subject by the

attempt to classify cases of acute meningitis according to their anatomical distribution; in this way suppurative meningitis has been distinguished as "vertical," and the epidemic disease has been called "cerebro-spinal"; but it must be clearly understood that any form of meningitis may be, and often is, cerebro-spinal in distribution, and suppurative meningitis, though it tends to affect the vertex first and chiefly, may nevertheless be limited to the base and spinal cord.

The ideal basis of classification is the bacteriological, but in the present state of our knowledge no complete clinical differentiation on the same lines is possible, so that for practical purposes it is convenient to group together under the head of suppurative meningitis those cases of acute leptomeningitis which, although infective in character, do not fall into clinical groups corresponding with their bacteriological differences, as happens in the epidemic, the posterior basic, and the tuberculous forms.

Etiology.—Suppurative meningitis is most common in infancy, but it occurs at all ages. There is no marked difference in the frequency with which the two sexes are affected. No particular seasonal variation has been observed, except in so far as the meningitis follows the seasonal curve of the infective conditions with which it is associated; the pneumococcal cases for this reason are commoner in winter and spring than at other times.

Suppurative meningitis occurs most often as a complication of pneumonia or empyema. The next most frequent cause is bone disease in connection with the ear. It occurs also as a complication of several infective diseases, especially erysipelas and pyæmia, including under the latter head malignant endocarditis; rarely it complicates smallpox, scarlatina, typhoid, and influenza, and still more rarely it has been seen in cases of nephritis; but in all these conditions it may be rather a sequela than a complication, and it is certain that sometimes at least in such cases the meningitis is not due to the same virus as the primary disease, but is pneumococcal or streptococcal in character, and is secondary to some pneumococcal or streptococcal lesion elsewhere, to which the primary disease predisposed. It may be due also to injury; sometimes it results from disease of the nasal cavities; and in infants a not very rare cause is sloughing of the skin over a spina bifida.

Bacteriology.—The micro-organism most commonly found in the meningeal exudation is the *pneumococcus*. In children fully two-thirds of the cases are due to the pneumococcus. This micro-organism also would seem to be the usual cause of the meningitis in

the very rare cases where this disease is primary. Where meningitis occurs as a complication of erysipelas or pyæmia the *streptococcus* is often found in the exudation, while in cases secondary to disease of the petrous bone a mixed infection is usually found, *streptococcus pyogenes*, and *staphylococcus aureus* or *albus* being present sometimes with *bacillus coli communis* and sometimes with the pneumococcus also. In some cases, even where the primary source of infection is pneumococcal, and cultures from the meningeal exudation show an almost pure growth of the pneumococcus, the streptococcus pyogenes, or staphylococcus albus or aureus is found to be present also, mixed infection having occurred. Cases have been reported in which the influenza bacillus or the typhoid bacillus have been found in the meningeal exudation, where meningitis occurred as a complication of influenza or of typhoid fever.

Symptoms.—In many cases, especially in infants, when the patient is already severely ill with the primary disease, the onset of suppurative meningitis is obscured by the previous symptoms, and this complication may even be entirely unsuspected until post-mortem examination reveals its presence.

More often, however, vomiting and convulsions occur at the onset, and in older children and adults delirium may be a marked feature. Sometimes from the beginning there is stupor, which gradually deepens into coma after a few days.

Headache is severe, and even when the patient is semicomatose the facies, with its anxious expression and knitting of the eyebrows, often suggests the continuance of pain. Retraction of the head is occasionally present, but is much less marked than in posterior basic meningitis.

Bulging of the anterior fontanelle is an early symptom in infants.

A fine tremor of the limbs, especially on movement, is often noticed quite early in the disease; paralysis of one or more limbs is sometimes present, and towards the end of the disease there is often rigidity.

Paralysis of cranial nerves is more common than in the posterior basic disease; squint is usually present. Slight nystagmus is sometimes seen, but much less often than in posterior basic meningitis. Optic neuritis is often associated with suppurative meningitis, but by no means always.

Vomiting is generally frequent throughout; the bowels are costive. The pulse and respiration are rapid and often irregular; the latter may be of Cheyne-Stokes' character. The temperature is usually high, but sometimes becomes subnormal towards the end.

Diagnosis.—It will be seen that in many of its symptoms suppurative meningitis resembles other forms of meningitis, and sometimes indeed the diagnosis is extremely difficult. There are, however, two points which serve to differentiate the suppurative form, both from the posterior basic disease and from tuberculous meningitis: first, its rapid course; suppurative meningitis is a disease of a few days, the onset of symptoms is sudden, their course is rapid: secondly, the presence of a source of infection, whether it be some local disease, such as empyema or ear disease, or some general disease, such as pyæmia. Where symptoms of meningitis are associated with such a source of infection, and prove fatal in less than a week, the diagnosis of suppurative meningitis is almost certain. From sporadic cases of the epidemic cerebro-spinal disease, suppurative meningitis is usually distinguished by the presence of some obvious source of infection, but in the rare cases of primary suppurative meningitis, where this point of distinction is lacking, the diagnosis may be impossible. Perhaps the presence of herpes or of a purpuric rash may point to the "epidemic" disease; certainly the prolongation of the illness beyond the tenth or eleventh day would be strongly against suppurative meningitis, but in most cases the only possible method of diagnosis is a bacteriological examination, and it may therefore be advisable in rare cases to make use of lumbar puncture.

In connection with ear disease there is often some difficulty of diagnosis, for, on the one hand, cerebral abscess may closely simulate suppurative meningitis, and on the other hand the meningitis which complicates ear disease is by no means always suppurative; in many cases it is tubercular. Cerebral abscess may be distinguished by its slower course, a normal or subnormal temperature, unilateral paralysis, sometimes aphasia, and in rare cases localised tenderness, but even such symptoms may be deceptive, for it sometimes happens, especially with ear disease, that suppurative meningitis remains for some time quite a localised process and may thus give rise to hemiplegic symptoms.

In tuberculous meningitis the onset is more gradual; the course is much slower; the temperature is generally lower than in the suppurative form; tache cérébrale, retraction of the abdomen, and slowness of the pulse, with irregularity, are more marked symptoms.

Prognosis.—In suppurative meningitis, whether secondary or primary, the prognosis is very bad. There is reason to believe that some cases of localised suppurative leptomeningitis in connection with ear disease have recovered where early operation has

been performed, but with this exception it is doubtful whether recovery ever occurs. It must be understood that no reference is made here to those sporadic cases of cerebro-spinal meningitis in which the diplococcus intracellularis is found; these are included under the head of epidemic cerebro-spinal meningitis and have a much more favourable prognosis. Suppurative meningitis is usually fatal in less than a week. The fatal result is very rarely delayed beyond the tenth day.

Morbid anatomy.—In very acute cases, where death has occurred within a day or two of the onset of the meningitis, the only abnormal appearance on the brain may be some excess of almost clear fluid in the pia-arachnoid, giving it a watery œdematous appearance, while at the same time there is some undue vascularity of the meninges, and perhaps a trace of grayish opacity along the vessels in the sulci. To this condition some observers have given the name of "serous meningitis." It differs only in degree from the later stages, in which the grayish opacity along the vessels becomes first yellowish exudation, then definitely purulent, until, in the most advanced cases a continuous sheet of greenish-yellow pus in the pia-arachnoid covers the whole surface of the brain. In many cases the exudation is most marked over the anterior two-thirds of the vertex, but it is seldom limited to the vertex. In most cases the base also is affected. Sometimes only a patch of purulent exudation is seen on the inferior surface of each temporo-sphenoidal lobe, but often the whole base is covered almost as thickly as the vertex. The spinal cord seldom escapes; the posterior surface, especially in the lumbar region, is affected earliest; later the whole cord is covered with exudation.

Although the inflammation is mainly in the meninges, it must not be forgotten that there is certainly in many cases, if not in all, some extension of the inflammation to the brain substance beneath, and in some cases this can even be appreciated by the naked eye as undue redness and vascularity of the superficial brain substance, which may show minute ecchymoses or even minute points of pus on section.

Rarely the meningitis is the only discoverable lesion, but in most cases, as already pointed out, some primary lesion is found elsewhere. In children this is usually empyema or thick lymph on the pleura, and it is not uncommon to find associated with the meningitis, in addition to the pleurisy, a purulent or sero-purulent pericarditis, and sometimes also peritonitis.

Treatment.—The only cases in which treatment is likely to

be of much avail are those in which meningitis is secondary to ear disease. Early surgical treatment in such cases has been successful, but it seems likely that where such a favourable result has occurred only a limited area of the pia-arachnoid has been affected. Operation is probably useless where the meningitis has already become generalised.

There can, however, be little doubt that much may be done in the way of prophylaxis. Careful antisepsis and timely operative measures in the treatment of otitis media would do much to reduce the mortality from suppurative meningitis. In empyema also, and suppurative pericarditis, any delay in operation probably increases the risk of meningitis. So long as pus or thick lymph is pent up in the pleural or the pericardial cavity there is a virulent culture of pneumococcus or other micro-organisms, which may at any moment give rise to a secondary infection of the meninges. It is important also to remember that even where an empyema has been already opened a separate collection of pus, perhaps only a drachm or two, may remain shut off by pleural adhesions, or enclosed in the mediastinal connective tissue, and such small collections may serve as the focus of infection from which a suppurative meningitis may result.

The treatment of suppurative meningitis in those cases which appear to be primary, or are not amenable to surgical treatment, resolves itself mainly into the treatment of symptoms, particularly the alleviation of pain. For this purpose the application of an ice-bag to the head or of leeches behind the ears may be tried; if these fail morphia should be administered. Nasal or rectal feeding will probably be necessary. In cases where there is great collapse and prostration early in the disease, as sometimes happens, stimulants, such as strychnine or alcohol, may be required, and hot-water bottles may be placed in the bed; but in this, as in other forms of meningitis, the patients often show a curious tendency to blister with the application of a degree of heat which would be quite innocuous in other diseases.

The use of antitoxic serum, either anti-pneumococcic or anti-streptococcic, according to the probable nature of the infection, is worthy of trial, but there is not at present sufficient experience to show how far such treatment may be of value.

G. F. Still.

INFLUENZA

Few diseases manifest themselves under guises so varied as influenza. Hardly an organ or system of the body that may not be its victim; hardly a symptom or subjective sensation it has not awakened. This almost infinite variety of manifestations not only makes diagnosis difficult, but leads to many obscure conditions being ascribed, without adequate evidence, to influenza, which has, so to speak, become the last resource of the baffled diagnostician. There are certain broad types of the disease which may be thus described:—

1. The simple type.—Here with suddenness occur the chilliness of fever, severe pains in the head, back, and limbs, rapidly followed by great nervous prostration. The face is flushed and the conjunctivæ suffused; the tongue is tremulous, indented, moist, and covered by a dirty white fur; the breath is fœtid. On examining the throat, the posterior pharyngeal wall is found red, injected, and often dry, the tonsils red and angry-looking, but not appreciably swollen; less often they are enlarged and their follicles plugged, as in a case of scarlet fever or tonsillitis. The pulse beats 90 or 100 to the minute—an acceleration moderate in proportion to the symptoms, and is soft and compressible, and liable to become dicrotic. The respiration is but slightly increased. There is either no cough or one that is dry and irritable, and having its origin in the throat and trachea. There are no abnormal physical signs in chest or abdomen. The skin is hot and dry to begin with, but later there is often profuse sweating. The urine is febrile. The pain in the head is severe, and on any attempt at movement is well-nigh unbearable; the eyeballs ache. The pains in the limbs are more marked in the legs than in the arms; the muscles and tendons are often excessively tender on manipulation, and the skin hyperæsthetic. The joints are neither swollen nor more tender than the condition of the periarticular structures will account for. The patient aches everywhere as if bruised, and in no position can comfort be obtained. He is restless and unable to sleep, except fitfully, and at times there is delirium. Further there is added an indescribable misery and depression, the whole constituting a feeling of illness which life could not endure, but for a brief space. The character of such an attack extends usually from two to five days, then the

temperature, which has varied from 100 to 103, or higher, falls to normal, or below it.

2. In the PULMONARY TYPE the disease is ushered in with the same symptoms of chilliness, fever, pains and prostration, but cough and embarrassed breathing early become prominent features. The cough is dry, especially troublesome at night, and exceedingly harassing—no cough more so; it will sometimes last almost continuously for an hour or more at a time, draining the patient's strength to the point of utter exhaustion. It may persist for weeks after the acute symptoms have subsided. The sputum is very scanty and tenacious, or may at first be quite absent. As the case progresses it will become rather more plentiful and change from the mucoid and translucent to the muco-purulent and opaque, but it often remains extremely sticky and tenacious, despite all efforts of treatment to loosen it.

The physical signs are slight in proportion to the severity of the symptoms and depend on the distribution and extent of the lung trouble. If the mischief is bronchial and confined to the larger and medium-sized tubes, the symptoms are milder than when it is broncho-pneumonic with the smaller tubes and alveoli involved. The more severe pneumonic condition is denoted by more rapid breathing, a weak rapid pulse of 120 or more, duskiness of the face, greater prostration. The physical signs of this influenzal broncho-pneumonia are peculiar and ill-defined, and in their absence of clearness and distinctness stand out in contrast with the definite signs of lobar pneumonia. The first feature to claim attention is a marked diminution of breath sounds, especially over the backs of the lungs, and a short, highly pitched, sticky râle, which is characteristic and conveys the same idea to the sense of hearing that the glutinous sputum does to the sense of sight. These special râles may often be brought out after coughing, over spots where the only sign before was diminished or absent breath sounds. There is a general impairment of resonance, more marked in some places than others, but no clearly defined area of dulness. Vocal resonance and tactile vocal fremitus are modified in no very helpful or constant way, but are diminished more often than increased. There may be here and there a patch of bronchial breathing, but it does not stand out as a usual or prominent sign. The next strikingly characteristic feature of these phenomena is the way in which they extend and change their distribution. Manifesting themselves more prominently at the bases, they creep from one part of the chest to another; perhaps one area will improve only for another

to be affected, or if one lung shows signs of improvement the other shows those of deeper involvement. It is this uncertainty as to the length of the illness, with its constant strain on the patient's strength, that makes this form of influenza so discouraging and anxious. If the case is tending towards a fatal issue the above signs extend over wider and wider areas of lung, but do not alter their features. At the same time the breathing becomes more rapid and shallow, the patient more distressed, and it may be delirious, the fever increases, the face appears more dusky, a semi-comatose condition supervenes, and, quickly following it, the end.

3. THE ABDOMINAL TYPE.—This form of influenza has been prominent in many less severe epidemics and is present in most.

The fever is moderate—often not above 100° F. The attack is characterised by the same suddenness of onset, and the same depression and prostration as in the former. Acute abdominal pain usually begins the illness and is followed by vomiting, and in some cases by diarrhœa as well. Anorexia is complete. Such an attack is often at first difficult to distinguish from other causes of acute abdominal pain, such as intestinal colic, gall-stone colic, gastralgia, and even peritonitis, but head or back pains, a sore throat or a cough make the true nature of the illness evident.

Course.—In no disease is the course of an attack so difficult to foresee. Fortunately a goodly proportion of the cases are moderate in severity and simple in type, and after three or four days of fever, headache, etc., the temperature will fall to subnormal, and the patient, feeling bruised and shattered, will slowly recover strength. No doubt, as with other specific diseases, there are slight, almost abortive, attacks, which run an even shorter course. Frequently symptoms will continue after the temperature has subsided, and this disproportion between the degree of pyrexia and the state of the patient is a characteristic feature. Or the temperature may keep up for two, three, or even more weeks, and, although the acute pains may go, the feeling and evidences of "illness" remain, perhaps creating doubt as to whether the case is not one of typhoid fever. Or what may begin with a simple attack will pass on into influenzal bronchitis or broncho-pneumonia, either directly, or in the form of relapse after a brief interlude of normal temperature; and, as already stated, this form of pneumonia is often very long-abiding. The clinical forms of the disease as described are not always sharply demarcated, but may follow or accompany each other.

Special symptoms, complications, and sequelæ—*Modifi-*

cations of the temperature.—All varieties of curve may be met with. Frequently highest at the onset, the acme may not be reached for several days. For some time the fever may be of a regularly intermittent type, accompanied by shivering or rigors, and followed by sweating—presenting a malariform character; or the greatest variety may be exhibited from day to day, occasionally the highest point being reached in the early hours. Now and then cases run their course with no rise of temperature—an apyrexial influenza. In such there is great prostration and depression, a subnormal temperature of 96-97° F., no acute pains, but a feeling of great illness and a sensation of sinking through the bed, a misery that defies description, and an utter inability to even hope or try to get better constituting a form of the disease perplexing to recognise, and one that recovers slowly and with difficulty. This occasional absence of fever recalls a similar and more frequent feature of diphtheria. Or, on the other hand, hyperpyrexia may set in, and this has been more particularly noticed in cases marked by severe cerebral complications.

Pulmonary complications.—Whilst the incidence of the disease specially tends to the respiratory passages, some part or other of which rarely escapes,—though the most prominent symptoms may be connected with other organs,—the greatest variety exists in the extent to which the several regions of the tract may be involved. The general nature of the affection is, primarily at least, that of a dry catarrh, often of very partial and limited distribution, with ill-defined physical signs.

The soil of the influenzal bacillus is congenial to that of the pneumococcus, and lobar pneumonia will often supervene in a case of influenza; pleurisy and empyema, the latter due to secondary streptococcal infection, are also met with. Influenza may awaken or reawaken phthisis. Gangrene, fibrosis of lung, bronchiectasis, all may have their origin in an attack of influenza.

Cardio-vascular complications.—Influenzal, like diphtheritic cardiac affections, for the most part have their origin in some vice of the controlling nerve mechanism which is due to the influenzal toxines; thus tachycardia and irregularity of rhythm are both late effects of influenza, and may last for very many months; or the pulse may be markedly slowed in the later stages. Acute dilatation of the heart may develop during, or at what is apparently the end of, an attack; it manifests itself subjectively by faintness and extreme weakness, and objectively by pallor, displacement of the apex beat, a rapid, irregular, and feeble heart action and pulse. It is always a grave,

though fortunately rare, occurrence, and, as in acute rheumatism, may be attributed to the direct effect of the toxin on the myocardium. Pericarditis is sometimes met with. There are grounds for thinking that influenza, although not a cause of endocarditis, yet favours in some way the development of ulcerative endocarditis.

Phlebitis and thrombosis of veins.—In the cases met with, the lower extremities are most often the seat, and the usual manifestations of pain, tenderness along the affected vein, and swelling are present, with the same obstinate slowness of recovery. Thrombosis of arteries, especially the popliteal, with subsequent gangrene of the limb, has been recorded.

Epistaxis, melæna, hæmatemesis, hæmaturia, and menorrhagia are examples of bleeding from mucous surfaces, and purpura has been frequently observed, either alone or in conjunction with other rashes. It may be noted that these bleedings are sometimes severe.

Œdema, general or confined to the lower extremities, not owing its origin to the condition of the heart or kidneys or to thrombosis, is occasionally a late effect. It varies considerably in degree from time to time, and may last many months. Its pathology is obscure, but is apparently toxic in origin.

Digestive disturbances.—Although clinically it is convenient to refer to an abdominal type of the disease, there are rarely, if ever, to be met with structural changes comparable to those found in the respiratory organs. The usual phenomena met with are anorexia, furred tongue, foul breath, constipation, or oftener diarrhœa, and not unfrequently vomiting. If the gastro-intestinal symptoms be severe, and especially if certain of the nervous complications develop, the resemblance to typhoid fever may be marked. Parotitis is of occasional occurrence. Jaundice, varying from the slightest tinting of the conjunctivæ to a general definite staining of the skin, has been noticed, with urobilinuria.

Spleen and lymphatic glands.—An enlargement of the spleen is sometimes noticed.

Besides the tonsillar glands, which are usually swollen and tender when the throat is involved, it is not unfrequent to find a more general enlargement of the glands of the neck, and even rarely of other parts of the body.

Nervous system.—The headache, frontal or general, and pain in the back, which characterise the onset of the disease in most cases, may attain an extreme degree. Insomnia also is frequent and distressing, and may persist long after other symptoms have subsided,

whilst delirium is not uncommon during the febrile stage. Vertigo is a feature of some cases. Loss of taste and smell are sometimes complained of.

Neuralgia is often severe and lasting. It is widely distributed, and only occasionally localised to the courses of particular nerves. Myalgia, particularly of the thighs and calves, is frequent. These pains are in large measure due to the condition of the nerve centres, degrees of peripheral irritation, which in health would pass unheeded, being brought up into consciousness and producing pain.

Neural troubles resembling organic disease either of the peripheral nerves, or of the spinal or cerebral centres, are common. Nervous symptoms, which at their inception perhaps suggest neuritis or myelitis, often prove to be caused by a functional toxic poisoning. At the same time neuritis, either multiple or local, does occur in the course of influenza, as in that of diphtheria, typhoid, and other microbic diseases. It is not selective, and shows no special bias for any particular group of muscles, like the diphtheritic form for the palate, and the alcoholic and lead varieties for the extensor muscles of the wrist and ankle.

Meningitis and myelitis, either local or diffused, are also among the rare effects, but may be due to a mixed infection.

Beyond these more easily defined effects, influenza will leave the nervous system bankrupt and exhausted. Weariness of the body and mind make all effort irksome and difficult; memory is bad, ability to think enfeebled, and there is an absence of that initiative and spontaneous desire to be up and doing which is so strong a feature of health. The enforced idleness brings with it no sense of ease or repose, and the patient feels gloomy and depressed. It is common to meet examples of people who, without having any illness that can be labelled, have for ever been ailing since an attack of influenza. Their power to stand up against the wear and tear of life seems gone, and they threaten to become a burden to themselves and to others. Passing to certifiable insanity, melancholia, with or without delusions, is by far the most common, and next to this is mania.

Otitis media.—This may appear with but slight warning. A sore throat is followed by intense ear-ache, which is often not relieved till the membrana tympani bursts, and pus is discharged. The condition will slowly improve, or may pass into a chronic condition.

Numerous *affections of the eye* may complicate influenza; among

those of more frequent occurrence are conjunctivitis, keratitis, and various ocular neuroses.

Skin affections.—Erythematous, urticarial, herpetic, purpuric, and rarely bullous eruptions, will make their appearance during the height of an attack, or during early convalescence. The erythematous rashes are the most common, and may be difficult to distinguish from those of scarlet fever or measles.

Renal complications.—A trace of albumen in the urine is not uncommon. A large quantity of albumen, with or without hæmaturia, may be present; sometimes it is accompanied by œdema and denotes nephritis, but more often it does not. Glycosuria is of occasional occurrence.

Orchitis sometimes arises, and it is said to do so in conjunction with parotitis.

Arthritic affections are rare, but met with. Influenza predisposes to rheumatoid arthritis.

The exceedingly wide range of manifestation here set forth confers the multiform character on the disease. How far all these phenomena are to be regarded as essentials of the malady, and directly attributable to the causal microbe is doubtful and the possibility of mixed infection should not be lost sight of.

Diagnosis.—Owing to its many-sidedness, influenza often presents difficulties in diagnosis. At its inception the high temperature and the onset might well suggest measles, scarlet fever, or pneumonia, or other specific fevers.

Where the characteristic rash and throat of *scarlet fever* appear on the second day all doubt is usually at an end, but we have to remember that these signs may both be present in influenza, and then the difficulties may be great. The points to consider are these, the rash of influenza is not punctiform, does not begin on the chest and extend like scarlet fever, is patchy in distribution, and fades and intensifies alternately, even from hour to hour. Further, it is sometimes polymorphic. The difference between an influenzal and scarlatinal throat is of great importance. The former is chiefly pharyngeal, while the latter chiefly shows itself in redness, enlargement, and plugging of the tonsils and redness of the soft palate. But when it is remembered that the tonsils are sometimes swollen and plugged in influenza, it will be seen how very difficult it may be to differentiate between the two diseases. The history of a previous attack diminishes the probability of scarlet fever.

From *measles* the difficulty of diagnosis arises during the first four days. The more marked catarrh of the nose and eyes of

measles on the one hand, and the definite pains of influenza on the other, will aid in the forming of a judgment. When the time for the appearance of a measles rash arrives, the difficulty is usually at an end, but it has to be borne in mind that a morbilliform rash may accompany influenza.

Diphtheria.—In so far as the diagnosis depends on the local condition, it is the same as that between tonsillitis and diphtheria. In the latter a cultivation from the throat will reveal the Lœffler bacillus.

Pneumonia.—The sudden onset, the hot dry skin, are features common to the two diseases. But in pneumonia, if there is pain, it is in the side, not in the head and back, the breathing is rapid, and there may be herpes of the lips. Further, signs of extensive lobar consolidation—dulness, marked tubular breathing, increased voice sounds—would be convincing evidence of croupous pneumonia, although the absence of these signs must not lead to a contrary opinion from the fact that the appearance of physical signs in pneumonia is often delayed several days. It must be remembered, too, that pneumonia is an early complication of influenza. The distinctions between influenzal and pneumococcal pneumonia are well defined. In the latter the distribution is lobar and clearly circumscribed; in the former it is lobular and ill-defined; in the latter there are tubular breathing and increased voice and breath sounds over an area of distinct dulness; in the former there are no such signs, but diminished breath sounds and sticky crepitations over ill-defined areas, slightly, but not distinctly, dull. An examination of the sputum for bacillus influenzæ should be made in cases of doubt.

When a case hitherto thought to be influenza develops shivering, rigors, hectic temperature and sweating, doubts may occur, and the possible existence of deep-seated suppuration, of pyæmia, or of malaria, be thought of. But the fact that influenza may develop malarial characters, and the early history of the attack, or the absence of primary or secondary foci of suppuration should lead to a right judgment.

Enteric fever.—This question arises at two stages of the illness—during the first few days when the evidences of influenza are perhaps ill-marked, and again when the fever extends into the second or third week. In the former case, doubt is felt at the commencement of the illness, and is usually set at rest by the fall of temperature and amelioration of the symptoms on the third or fourth day; while in the latter case doubt develops later in the physician's mind, and a diagnosis of influenza which he at first adopted with

certainty, becomes, as the days roll by, more and more open to question. Since influenza and typhoid are both diseases whose positive evidences are sometimes lacking, it will be readily understood that a confident diagnosis may at times be impossible. The points of distinction to attend to are these. The pain of typhoid is chiefly confined to the head, while that of influenza is as marked in the back and legs; the tongue of typhoid during the first week or ten days resembles that of influenza, but, unlike influenza, changes to a dry, glazed, cracked appearance towards the end of the second week; in typhoid, a distended elastic abdomen and a palpable spleen are common, while in influenza they are uncommon. The presence of the typical diarrhœa is in favour of typhoid, but it is important to bear in mind that its absence is not evidence to the contrary, for constipation is as frequently met with in that disease. The same holds good with regard to rose-coloured spots—their appearance goes far to determine a diagnosis of typhoid, but their absence does not point strongly to influenza, considering that they may be long delayed, or even absent altogether. By the middle of the second week the general condition of a typhoid patient, as evidenced by the appearance and wasting, mental dulness and apathy, is distinctive, and becomes more accentuated with the lapse of each subsequent day. On the other hand, with influenza, unless aggravated by some grave complication, there is, although great weakness, no such marked wasting, and the patient continues to take notice of his surroundings. And, lastly, Widal's serum test should be employed, remembering that, though evidence of importance which should contribute to the forming of a judgment, it is not infallible.

Gastro-enteric influenza is liable to be confused with other causes of sudden diarrhœa and vomiting, such as poisoning, either ptomaine or metallic. In poisoning the subnormal or normal temperature, the marked and early collapse, and the history lead to a right diagnosis. But sudden pain and vomiting may be the only symptoms, and then this form of influenza has to be distinguished from other causes of acute abdominal pain, such as the various forms of colic, and even peritonitis.

In many of its features influenza resembles *dengue;* the sudden onset, severe pain in head and back, nervous prostration and high temperature, are alike in both. But in the latter affection the joint pains are more constant and tend to last longer, and a roseolar exanthem starting in the hands and spreading to the trunk, followed by desquamation, is usually to be seen.

Morbid anatomy.—Characteristic changes are few, and are almost entirely confined to the pulmonary type of the disease. The trachea and bronchi are red, injected, and contain tenacious mucus. The lungs show the changes of a broncho-pneumonia; they are imperfectly ærated, and on squeezing them a thick muco-pus exudes from the bronchioles. Disseminated patches of consolidation of varying density are seen. They are smooth and of darker hue, and interspersed amongst them are areas of aerated and collapsed lung tissue. Or through coalescence of the lobular areas the lung may present some resemblance to lobar pneumonia, but its section has not the homogeneous granulated appearance of that condition. Under the microscope the changes seen are those of broncho-pneumonia. There have also been described small areas of purulent infiltration, the centres of which are packed with round cells. Pleurisy is sometimes found in conjunction with the above changes. As in other acute infections, the spleen is frequently somewhat enlarged and soft.

Etiology.—Influenza is a communicable disease propagated from person to person. The critical study by Dr. Parsons of the 1889-1892 epidemics pointed strongly to the conclusion that the spread of the disease was conditioned by human intercourse and was not dependent upon air-borne infection. The rate, and still more the mode of extension strongly supported this view, and, as will be seen below, what we know of the bacteriology of the disease leads to a like conclusion. Several distinguished physicians of the eighteenth century taught that the disease was contagious, but until the investigations which sprang from our recent visitations, the teaching of the nineteenth century has favoured an air-borne theory of infection. This view owed much of its strength to the lightning-like rapidity with which the disease struck down large numbers of people within a very short space of time. This feature, in common with some others, is the combined effect of a short incubation period, an early infectiousness, a widespread susceptibility and early unrecognised cases. **The incubation period** is two to six days, and perhaps at times the limits are wider. Infectiousness commences very early, often within the first twenty-four hours, and it may be before the character of the disease has declared itself. It persists as long as the acute symptoms, and in the pulmonary form as long as the catarrh lasts, and, judging by the presence of Pfeiffer's bacillus, even longer. The widespread susceptibility is due to the very imperfect and transient immunity conferred by a previous attack. Indeed, with some people one attack

predisposes to, rather than protects from, another. Granting, for the sake of illustration, an incubation period of two days, a power of infection commencing at the end of the first day's illness, and that each case each day infects two or three people, a simple calculation will show that a single case will have become converted into many hundreds after a very short time.

Bacteriology.—The *bacillus influenzæ* was discovered by R. Pfeiffer in 1892. It occurs singly or in clumps as very minute rods 1.2 $\mu \times 0.4\ \mu$, devoid of capsules. The bacilli are found abundantly in the respiratory tract, often existing in pure culture in the sputum either in or among the leucocytes. In the nose, mouth, and pharynx, they are present, but admixed with other microbes. They have been obtained from the discharge in cases of otitis media, and from five or six cases of fatal meningitis. In the blood it is the exception to find them, and it is probable that when present they do not survive long. They are found in no other disease.

To search for the bacilli in the sputum, select for choice the small greenish-yellow masses in the latter, make cover-glass preparations, dry and stain for a quarter of an hour in Ziehl-Neelsen's carbol fuchsine (1 in 12 of water), afterwards wash, dry and mount in Canada balsam. The poles of the bacilli stain, while the middle portions do not, so that at first sight they show a resemblance to diplococci if isolated, or to streptococci if several are placed end on.

Artificial cultures are not easy to make or preserve. The best medium is blood agar, and, if a streak cultivation with sputum be made, after twenty-four hours at the body temperature colonies will appear consisting of minute transparent dots like drops of dew. These colonies will not live long, and if it is desired to preserve the strain, subcultures have to be made every second day.

The vitality of the bacillus is low, its maximum temperature is 42° C., and its minimum is 25° C., while it thrives best at the normal temperature of the human body. It will not live beyond two days, either in the dry state (*e.g.* dried sputum) or in water, but in moist sputum its vitality extends to two or three weeks.

Animals are for the most part immune, and numerous attempts to reproduce the disease in them have yielded negative results. Although this is a weak link in the chain of evidence, there is little doubt that the bacillus influenzæ holds a causal relationship with the disease. The bacilli do not circulate in the blood, but find their home in the respiratory tract and other places congenial to their growth. Here the toxines are produced, and, entering the

circulation, work havoc in different tissues, but especially in nerve-cells and fibres, thus resembling diphtheria.

The mode of propagation of influenza, the low resisting power of the bacilli, the small range of temperature within which they flourish, their inability to live but a short time in a dry condition or in water, and the immunity of animals, all lead to the conclusion that the disease is mainly spread from person to person, either directly or mediately by means of fomites. It now can be understood why it is that such factors as climate, soil, altitude, occupation and sanitary surroundings have little or no bearing on the incidence of the disease.

There are, however, many problems connected with the spread of influenza as yet unsolved. Why, for instance, should the disease spring up simultaneously in epidemic form in widely separated regions of the earth's surface? Thus the 1891 epidemic began simultaneously in the month of March in Yorkshire, Wales, and the United States. Why, again, are the visitations intermittent? There must be external conditions of the nature of which we are ignorant, acting over wide areas, that either increase the life activity and virulence of the microbe, or the vulnerability of the human beings exposed to its action.

Prognosis.—The severity of the disease and therefore its mortality vary greatly in different epidemics. At all times a large proportion of the deaths is due either to influenzal broncho-pneumonia or supervening pulmonary complications. With the simpler forms of the disease, which constitute the majority of the cases, given previous good health and efficient treatment recovery is to be expected. Amongst the aged and those who are weakly even the milder forms of the disease afford cause for anxiety, and recovery, if such results, is often incomplete. As regards the late effects of influenza, although they may linger—it may be for months or even years—with a most discouraging persistence, yet, if there is no organic lesion and the patient was previously of sound constitution and is not old, ultimate restoration to health is the rule.

Prophylaxis.—It is most important for the fact to be recognised that influenza is an infectious disease whose spread can be checked by isolation. In institutions like workhouses, whose normal relations with the outside world are restricted, and in which strict isolation of first cases is carried out, it is possible to protect the inmates from infection even when the disease is raging in their immediate neighbourhood. When, however, on the one hand, the peculiar features of the disease, and on the other hand the

conditions of social life are considered, it must be admitted that isolation has its limitations and can only mitigate but not entirely prevent an epidemic. The question then arises—What measures that are practicable can be taken by a community to check the spread of the disease?

(1) As far as possible prevent the contact of the uninfected with the infected. Thus, people who are down with the disease should remain indoors, not only for their own sakes, but for the sake of others. It might be desirable to close schools; and large assemblages of people, as in theatres and churches, should be avoided. (2) Good ventilation and cleanliness of street, house, and person are important. (3) The sputum should be kept moist. (4) The room and clothing of a patient should, when practicable, be disinfected at the end of the attack. In schools isolation should be continued for at least a week after the subsidence of symptoms.

Treatment.—The underlying aim of treatment should be "to help him to bear it." There is not only the crushing effect of the original onslaught to be dealt with, but it is impossible to tell what the duration of the illness will be, or what complications will supervene. What begins as an apparently mild, develops into a severe attack, and some complications are as prone to follow mild as severe invasions. What has to be done is to save the nervous system the wear and tear—the devitalising effects of pain and distress, and this may be achieved by measures that make for comfort, and therefore for strength, and measures that relieve discomfort.

Bed is the only place for the victims of influenza, and it cannot be too strongly insisted that the need for bed in a mild case of this disease is as urgent as in a mild case of diphtheria. Many fatal results have followed the neglect of this precaution.

Food.—In the early stages, milk and meat-fluids are all that the patient wants, or that it is useful to give him. As soon as the more urgent symptoms of illness subside, it is well to try and cautiously extend the dietary by tempting morsels of easily-digested food, such as custards, jellies, oysters, white fish, boiled chicken, sweetbread. And here it may with advantage be mentioned that a remnant of fever and a persistence of fur on the tongue need not be a bar to solid food. Indeed, their disappearance is often promoted by the change from liquid diet, partly perhaps because of the encouragement the patient feels on returning to a food more resembling that of health.

Free action of the bowels should be secured, but severe purgation avoided.

To diminish the pains.—Phenacetin, methylacetanilide, phenazone and allied drugs are of great use. The first is, as a rule, the best, and is given in powder, gr. 8 to 10 for an adult every three or four hours, according to the severity of the symptoms. If the circulation is depressed, or the patient weakly, it is well to combine caffeine gr. 2 with each dose of phenacetin. Methylacetanilide is conveniently administered in mixture — 4 grains for a dose, put up with tinct. aurantii to dissolve and flavour it. Salicin and salicylates are sometimes employed with the same objects as the foregoing, but in efficiency they are inferior. Sometimes a saline diuretic and diaphoretic mixture affords most relief.

In a disease productive of so much weariness and distress, it is of the highest importance to give the body some rest and the mind some forgetfulness. Sleep should be secured by the exhibition of *hypnotics* alone, or in combination with anodynes. Of these trional and sulphonal are the most suitable; they have not the depressing effects of chloral nor the persistently unpleasant taste of paraldeheyde. Trional has an advantage over sulphonal in that its latent period is shorter. Where there is acute pain, a hypnotic will not alone secure sleep, but needs the assistance of the anodyne effect of opium. A good combination is 10 to 15 grains of Dover's powder with 20 grains of trional administered in a cachet. Or the opium may be given as a morphia injection and the trional or sulphonal by the mouth. In one acute form only of influenza must the use of morphia be avoided or employed with great caution, namely, in the broncho-pneumonic. There the great tenacity of the sputum and the diffuse distribution of the inflammation render its use hazardous.

Stimulants.—These are not required if the form of the disease is simple and the subjects are robust. But if the attack is prolonged or of a severe type, and if the patient is either old or of weakly constitution, alcohol is both necessary and desirable. Where there is evidence of cardiac and respiratory failure ammonia and ether, or better, perhaps, hypodermic injections of strychnine (gr. $\frac{1}{60}$ to $\frac{1}{30}$), or caffeine (gr. 2), should be prescribed even to several times in the twenty-four hours.

The dryness and soreness of the throat usually require relief; an inhalation of carbolic acid partially secures this—℞ Acidi carbolici liq. Aq. āā ℥ij. Misce. One drachm to the pint of hot water. Inhalations of pumiline and Tinct. Benzoin co: may also be employed. Carbolic acid may also be used as a gargle. ℞ Acid

carbol. liq. ℥i., Glycerine ℥i., Inf. Rosæ acid: ad ℥iij. Mix and dilute with equal parts of hot water.

It is a great comfort to the patient to have the furred tongue and the mouth cleaned. This is best done by means of cotton wool held by dressing forceps and dipped in the following solution— ℞ Acid carbolici liq. ℥ss., Hydrogen peroxidi ℥ij., Glycerini boracis ℥i., aquam ad ℥vi. Misce. Used as it is, or diluted with a little warm water. This preparation may also be used as a gargle or spray.

Where the *pains in*, or more often round, *the joints* are severe and persistent, relief may be given by glycerine of belladonna and moist heat locally.

Influenzal broncho-pneumonia is exceedingly resistant to treatment. Its irritable cough and its sticky sputum often seem but little affected by such expectorant remedies as ipecacuanha, potassium iodide, ammonia, squills, etc. Turpentine, 5 to 10 minims for a dose, in gelatine capsules every four hours, sometimes does good, but when giving this drug the urine must be carefully watched. The necessity for caution in the use of opium in this condition has already been referred to. External applications in the shape of poultices not only afford comfort but help to loosen the sputum.

For the gastro-intestinal symptoms nourishment should be restricted to milk, with soda or barley water given in small quantities frequently. If there is vomiting a blister to the epigastrium will often stop it, and hot applications will allay abdominal pain. For drugs, sodium bicarbonate, sal volatile, and spirits of chloroform, with the addition of morphia to check the pain and diarrhœa. If vomiting is a persistent feature acid hydrocyanic: dil: or the agreeable tinctura pruni virginianæ, may be added to the above. Bismuth is also employed, but is of less use than in simple gastro-intestinal irritation.

The malarial type yields well to quinine given in 3 to 5 grain doses three or four times daily.

During convalescence the patient should not be allowed to get up till the temperature has been down for some days, and then only with caution, always bearing in mind the liability to relapse. The diet should be generous and the appetite encouraged, and a little wine with the food should be allowed. Quinine is now the drug most generally useful, alone or in combination with strychnine. As recovery is approached iron should be added. Where possible a change of air should always be advised, and after severe attacks should be strongly insisted upon. It is only in this way that

recovery is consolidated and the long and varying train of sequelæ avoided. The treatments of the late effects of the disease do not call for detailed description. A word of warning, however, is needed concerning the insomnia, the various neuralgias and distressful feelings that sometimes tarry so long and wearily. On no account must opium be employed for their relief. This drug is as bad at this stage as it is often good in the first and acute stage. Hypnotics, too, like trional and sulphonal, must be given cautiously.

BERTRAND DAWSON.

GLANDERS

SYN. FARCY, EQUINIA, MALLEUS

An infectious disorder peculiar to the horse and ass, though transmissible to other animals, and also to man.

In the majority of cases of human glanders the patient acquires the disorder directly, by inoculating a sore or wound of the skin or mucous membrane. In other instances the contagium seems to gain entrance through the respiratory mucosa, the tonsils, or the alimentary canal.

Nearly all the recorded cases have occurred in males, and in those who are closely associated with horses, such as stablemen, grooms, knackers, etc.; but occasionally the infection has been transferred from man to man, and the malady has been acquired in the laboratory.

Bacteriology.—The actual exciting cause is a schizomycete, *bacillus mallei*, a microbe about the same size as, but rather thicker than the tubercle bacillus. Though an ærobe, *B. mallei* is also a potential anærobe. Its cultural appearances in glycerin-agar and blood-serum are sufficiently distinctive, but on potato the growth is quite characteristic. On this medium at incubation temperature the growth is at first honey or amber yellow in hue, afterwards darkening to brown. The microbe is best stained with phenol-fuchsin or with phenol-methylene blue. It does not stain by Gram's method. From veal broth cultures, its specific metabolic product, mallein, is obtained by filtration. This is used for diagnostic purposes, and when injected into glandered animals it excites a marked local and

general reaction. Another experimental test is afforded by injecting pure cultures into guinea-pigs, whereby a glanderous caseation of the testicles is almost invariably determined.

The average **incubation** period is from three to five days, but it may be shorter, and incubations of fifteen to twenty days are known.

Symptoms.—The onset of the disease is usually marked by a rigor or frequent shiverings, malaise, headache, pyrexia, hot, dry skin, by general pains, especially marked in the joints and muscles, and by prostration.

The febrile symptoms are followed by an eruption which rapidly appears when the infection is the result of direct inoculation, but may be delayed when there is no definite local origin. The inoculation site swells, pustules form, and thereafter, breaking down, discharge a fœtid ichorous pus. Swellings which rapidly suppurate may appear in other parts of the body, chiefly on the skin, muscles, mucosa of the nose, and in the lymphatics and lymphatic glands. In many cases there is a specific pneumonia, a purulent arthritis, and in very severe cases an erysipelatoid tumefaction of the face. Such acute cases last for about a fortnight. Chronic cases continue for weeks, and may drag on for months. In these the febrile phenomena are less severe, and the anatomical lesions less frequent and often indolent. Yet these chronic cases may terminate in acute glanders.

The clinical pictures presented by glanders vary much as to the duration of the disease and the extent and distribution of the anatomical lesions. For descriptive purposes the disease has been subdivided into acute and chronic glanders, and acute and chronic farcy. The distinction made between glanders and farcy refers to the greater extent to which the respiratory system is affected in the former and the prominent position taken by the skin in the latter, the so-called *farcy buds* being nothing more than either the swollen lymphatic glands or the morbid collections in the cutaneous lymphatic vessels. A perusal of recorded cases will, however, show that no distinct line can be drawn between the two even clinically, and will convey the notion that glanders is a specific disorder on pyæmic lines, characterised by more or less febrile phenomena and by caseating, suppurating or ulcerative lesions in skin, mucous membrane, muscles, lungs, etc.

In many instances the naso-pharyngeal mucosa is little if at all implicated. But should the mucosa of the nasal passages be affected by continuity or by metastasis, a discharge, at first mucoid, rapidly becoming purulent or saniopurulent, flows from the anterior and

posterior nares. This glanderous ozæna may infect the lungs and alimentary canal. The inflammation of the lungs is indicated by dyspnœa and by saniopurulent expectoration, the physical signs of pulmonary consolidation being frequently absent. Infection of the intestine is indicated by diarrhœa and offensive stools.

In chronic cases the original infection site may present the aspect of an intractable chronic ulcer from which proceed the thickened lymphatics and their swollen glands. In the majority of the recorded cases the virus has been inoculated on a sore or wound, but there are many instances where no such local infection has been demonstrable. In these the incubation period seems to have been longer, and after the general febrile symptoms have declared themselves the disease has become diagnosable by the advent of a vesicular eruption rapidly suppurating, by the occurrence of intramuscular abscesses, by a fœtid ozæna, or by the specific pneumonitis.

The character of the pyrexia is variable; it may be continuous or of the remittent type; it may be slight or severe (104° or higher).

A positive **diagnosis** of glanders is at first often difficult. Considerable assistance will, of course, be received from a knowledge of the patient's occupation and a possibility of contact with the virus. In chronic cases one of the most prominent features is old-standing ulcerations of the skin, and such sores have more than once been mistaken for those of tertiary syphilis. The induration and thickening of the lymphatic glands and vessels in connection with the sore may help to guard against this error.

When the disease is suspected a diagnosis may be made by bacterioscopic examination of the contents of the pustules, of the abscesses or of the discharges; by the characteristic cultural appearances of the bacillus, especially on potato; by inoculation of the peritoneal sac of guinea-pigs with pure cultures; by means of the serum test or by the reaction to mallein which consists of the chemical products derived from the artificial culture of the bacillus mallei, subcutaneous injection of which causes a reaction similar to that produced by tuberculin in persons suffering from tuberculosis.

The **prognosis** is always bad. Nearly all the acute cases are fatal, and of the chronic ones many terminate as acute glanders.

Of the chronic cases about 50 per cent are stated to recover, and the issue is the more favourable according as the symptoms are slow and indolent and the course of the malady protracted. Yet when they do recover a permanent condition of debility, general or local, may remain.

The general **treatment** of glanders resolves itself into maintain-

ing the strength of the patient by means of suitable and nourishing diet and by stimulants. Drugs are of little avail. Mercury has been exhibited both internally and by inunction, but quinine and iron have more repute.

The most effective part of the treatment of glanders is surgical and antiseptic. The pustules, sores, and abscesses should receive constant and energetic attention, the results being the more satisfactory according as the cases are less acute and more chronic.

It is hardly necessary to point out that the dressings, soiled clothes, etc., should be carefully disinfected, or, what is better, burned.

R. G. Hebb.

TUBERCULOSIS

Tuberculosis is a specific infective disease set up by the action of a special virus, this last being a micro-organism now well recognised and distinguished as the tubercle bacillus. This bacillus, either directly, or by means of chemical products due to its presence, causes a special form of inflammation of the tissues, resulting in the formation of what is known as acute miliary tubercle or tuberculous nodules.

The present article deals with tuberculosis generally, its modes of invasion, its methods of local increase and extension to other organs, and its distribution throughout the body. For its effects upon the separate organs, and the symptoms resulting from them, reference must be made to the articles dealing with the diseases special to those organs.

Bacteriology.—The *tubercle bacillus* can be readily demonstrated in the sputa of tuberculous subjects, and is commonly found in the urine, pus, and other secretions from parts affected with the disease. It can also be shown in sections cut from the affected tissues. The bacillus is a motionless rod with rounded ends, about one-half the diameter of a blood corpuscle in length, and about one-sixth of its own length in thickness (Plate II.). The bacillus is chiefly recognised from its behaviour with certain aniline dyes. When a preparation containing it is stained with carbol-fuchsine and afterwards treated with dilute mineral acids, these last remove the colouring matter from all but the bacilli themselves, which then sometimes show a beaded structure with alternate coloured and uncoloured

portions. Whether this beading is due to spore formation or not is as yet undetermined. The leprosy bacillus is the only other pathogenetic organism at present known with a similar property of retaining its colour when treated in this way. (The caseous secretions of the glands of the vulva and glans penis frequently contain a bacillus which closely corresponds to the organism of tubercle and leprosy in its behaviour to carbol-fuchsine and acids, though it is stated that alcohol discharges the stain sooner in the former. This fact should be remembered when examining urine for the tubercle bacillus.) The ordinary method of showing the presence of the tubercle bacillus is to first stain the suspected preparation with carbol-fuchsine, then to decolorise with a dilute mineral acid, and finally to stain again with methylene blue, when the bacilli retain the red colour of the fuchsine and contrast strongly with the blue of the rest of the preparation. The bacilli can be cultivated on several special media at temperatures between 98.5° F. and 102° F., but in every case the growth is essentially a slow one. Except when grown in this way, the bacilli have no power of extra-corporeal increase. They can, however, even when dried up, retain their vitality for a long period of time.

Histology.—In whatever way the virus may have gained an entrance, the initial lesion is a miliary tubercle, and the successive formation of such miliary tubercles is the essential and constant feature of the complaint. Under the microscope this tubercle is found to be made up of three separate zones or layers. The innermost zone consists of one or more large many-nucleated cells, with prominent branching processes—the so-called giant cells. Surrounding the inner zone is a layer of epithelioid cells. Outermost of all is a layer of smaller lymphoid cells. These three layers of cells are not always present, and a tubercle may be composed of two only of them, or even of lymphoid cells alone.

A single tubercle proper, such as that just described, is hardly perceptible by the naked eye. Commonly, however, several of them are aggregated together, and it is such collections of them that give the characteristic visible features of the complaint, and to which the term tubercle is ordinarily applied. Before undergoing any retrogressive change, these collections of tubercles tend to form little tumours of a definite size, this size varying somewhat in the different tissues of the body; and it will be convenient to follow the usual custom and speak of such collections as tubercles simply. A tubercle, in this sense, is usually a small globular body, about one-twelfth of an inch in diameter, pearly gray or yellowish in colour, and some-

what translucent in appearance (gray granulation). It is strictly extra-vascular, and capillaries can be traced up to its very margin, but never into its substance. Sooner or later the presence of tubercles is accompanied by inflammation of the tissues containing them, both in their immediate neighbourhood and in distant parts.

After reaching maturity, tubercles are liable to two forms of degenerative change—the caseous and the fibrous. Both processes are usually combined to some extent, although the amount of the one generally predominates over the other.

(*a*) *Caseous degeneration* is a form of dry necrosis which, owing probably to its non-vascularity, starts primarily in the tubercle itself, but afterwards involves the surrounding inflammatory products as well. The resulting formation is a homogeneous yellowish mass, somewhat of the consistence and appearance of soft cheese, which was formerly known as "yellow tubercle." Under the microscope the degenerated mass is found to consist of shrivelled corpuscles intermixed with granular *débris* and fat. By the coalescence of the separate tubercles caseous masses of considerable size may be formed, more especially in situations having no connection with the free surfaces of the body. In active cases the caseous masses may be surrounded by recent miliary tubercles. Further changes may bring about the softening of the caseous material with the formation of an ulcer or an abscess, according as the tubercle occurs on a free surface or in a closed cavity. When the caseous masses do not soften, and remain obsolescent, they are apt to take up lime salts from the blood, and so become transformed into cretaceous material.

(*b*) The other form of tuberculous degeneration, the *fibroid*, is a frequent feature in tuberculosis of the pleura and peritoneum, and not very uncommon in the lungs. Here the inflammatory products surrounding the tubercles, instead of undergoing caseous degeneration, are transformed into fibrous tissue, which is often of considerable thickness and extent. The fibroid change is in the direction of the cure of the complaint, for the fibrous tissue resulting from it may interpose an effective barrier against the spread of the virus. In such a change the actual tubercles themselves generally persist as fibrous nodules, or as small cretaceous masses.

Tuberculosis in its clinical aspects presents itself in two forms: a *chronic* one, in which the complaint is mainly confined to one or two organs or set of tissues, spreading mainly by direct extension or by means of the lymphatics; and a more or less *acute* one, *general tuberculosis*, in which many organs are simultaneously attacked; in this variety it is evident that the virus must have

been carried by means of the general blood stream. It is this generalised form which is most frequent in infancy and early childhood.

Invasion and distribution.—Of the modes of entrance of the bacilli into the human body only three need be considered—inoculation through a breach of the skin, inhalation through the air passages, and introduction into the alimentary canal along with food.

The first mode, *inoculation through a breach of the skin*, is extremely rare; examples of it being the occasional occurrence of warts on the hands of those making post-mortem examinations on tuberculous subjects.

The second mode, *through the agency of the air passages*, is by far the most frequent one by which the disease is contracted. It is by means of the virus inspired with the air, and, but less frequently, through the agency of food, that the glands in the neck, the lungs, and the bronchial glands are usually infected, and it is in few cases of tuberculosis that one or more of these structures is not involved.

The *glands in the neck* are infected by the bacilli gaining entrance to them from the parts about the mouth, more especially the lymphoid tissue of the tonsils, and the pharynx. That the organisms can gain an entrance to the glands when the parts inside the mouth are in a healthy state is perhaps true, but that an inflammatory condition of such parts assists their entrance is more than probable. Once in the glands the bacilli may multiply with the resulting formation of miliary tubercles, followed in due course by inflammation, necrosis, and caseation. Such is the origin of the familiar and well-known "strumous" or "scrofulous" glands in the neck. (Since it is now proved that the condition expressed by these terms is due to the tubercle bacillus, their retention is only justifiable on the ground of clinical expediency and not on that of pathological distinction.) Here the process may stop, and the tuberculous glands may persist for many years as chronic indolent swellings. Often the inflammation goes beyond this point, and a tuberculous abscess forms in the neck. In other cases the necrotic process in the glands involves the walls of the blood vessels, generally a small vein, with the result that the bacilli gain an entrance into the general blood stream. Once in the veins the bacilli are carried along by the venous current towards the lungs, and either find a lodgment in the pulmonary tissues or pass through the capillaries of the lungs to infect distant organs. It may be remarked here that it is almost certain that the bacilli, whilst in

motion with the blood stream, have no power of multiplying, and only in rare instances have they been discovered in the blood itself. For their increase a condition of rest is probably an essential. Another consequence of tuberculosis of the glands is that the inflammatory process sometimes leads to rupture of their capsules, with the result that the bacilli gain an entrance into the lymph current and thus infect other glands, or pass into the general blood stream by way of the thoracic duct. Amongst these other glands those at the root of the neck surrounding the apices of the lungs, and the tracheo-bronchial glands, are of prime importance, as their infection may lead by direct extension to disease of the lungs themselves.

From the pharynx the bacilli may gain an entrance into the *tympanum* by way of the Eustachian tube, and tuberculous disease of the ear is frequent in children and especially in infants. The usual result of the presence of the organisms is suppuration in the tympanic cavity, which may be followed by caries or necrosis of the petrous portion of the temporal bone and tuberculosis of the brain or its membranes. Much more rarely tuberculous meningitis is due to disease of the bones at the base of the skull; the bacilli having reached them by the route of the nasal passages.

In the *lungs* the bacilli gain an entrance with the inspired air, and their first effects are exercised upon the finest bronchial tubes. The apices of the lungs are the parts most often attacked, owing doubtless to the fact that they are the least expansile portions, and that the bacilli are most likely to attain a footing where the air is more or less stagnant. From primary foci in the finer bronchial tubes the disease has a tendency to spread in one of two directions, or in both simultaneously, viz. along the bronchi to the alveoli of the lungs, or else from the bronchi into the surrounding tissue and thence by direct continuity into the general connective tissue of the organ. In both cases there is progressive formation of tubercles and inflammation corresponding to the nature of the structures invaded. Besides spreading by direct extension in these directions, the complaint may attack more distant parts through the agency of the blood vessels and lymphatics. By the implication of the walls of the former, the bacilli may enter the blood stream, and develop fresh miliary tubercles in the general connective tissue of the lungs, corresponding closely to the ramifications of the terminal branches of the pulmonary artery. Fresh foci of infection, too, can often be traced in the lung tissue along the course of the lymphatic vessels on their way to the bronchial glands. These last are invari-

ably affected as well as the lungs, and it is only in exceptional instances that any tuberculous disease of these glands is not accompanied by demonstrable affection of the lungs as well. The effect of the disease in the bronchial glands is the same as in that of the glands of the neck, and the affection of the bronchial glands may be the means of spreading the disease to the lungs or to more distant parts, either directly by means of the blood vessels, or indirectly by the route of the thoracic duct. In exceptional instances, too, an affected gland may ulcerate into a bronchus, and the released bacilli may set up fresh foci of the complaint in many parts of the lung corresponding to the terminations of the finer bronchi. In other cases the disease spreads to the pulmonary tissues from the glands surrounding the bronchi in their passage to the lungs, and some authorities state that this mode of infection of the lungs is the commonest one in infants and young children.

The *pleura* interposes a barrier, more or less effective, against the spread of the disease into its cavity, and there may be extensive disease of the lungs with entire freedom of the pleura. As there is in fact no direct communication between the lymphatics of the pleura and those of the lungs, the pleura can only be infected by a breach of its surface through necrosis or other means. A secondary, non-tuberculous, pleurisy usually, however, complicates pulmonary tuberculosis of any great extent. In general tuberculosis gray miliary tubercles are frequently found on both the visceral and parietal pleural surfaces. Not infrequently, too, the first clinical manifestations of tuberculosis are exhibited in the pleuræ. It is now almost universally admitted that simple, primary, serous pleurisies are generally tuberculous in origin. However rapidly and apparently completely the victims of such pleurisies recover, statistics prove that the majority of them die before three years are over with undoubted tuberculous disease of the lungs and other organs.

Tuberculosis of the *pericardium* is seldom found except as the result of the general disease when many organs are involved.

Tuberculous disease of the *larynx* is nearly always secondary to disease of the lungs, and is probably due to infected sputa becoming lodged in the folds of the larynx.

In the third mode of entrance into the body, *by way of the alimentary canal*, the bacilli can readily reach the stomach and intestines by being swallowed with the saliva or sputum, or by the use of infected food. Modern research has proved beyond question the extreme frequency of the presence of the bacilli in ordinary

household milk and butcher's meat. It might be expected, then, from this fact that primary tuberculosis of the stomach and intestines would be of frequent occurrence. Fortunately this is far from the case, and primary tuberculosis of the intestinal mucous membrane is a rare event. Too much stress, then, has possibly been laid upon the frequency of infection through the agency of food by some recent authorities in their laudable attempts at controlling the disease. There can be no doubt, too, that cases of tabes mesenterica, *i.e.* tuberculosis of the mesenteric glands, are vastly exaggerated in frequency in the death returns. The comparative freedom of the intestinal tract from infection due to food is no doubt due to some destructive action of the gastric and intestinal secretions on the bacilli. Rare as a primary disease, tuberculosis of the intestines is far from uncommon as secondary to tuberculosis of other parts, most frequently that of the lungs. There is every reason for believing that in this case infection is incurred by the swallowing of tuberculous sputa. It is possible that in this instance the bacilli are protected from the destructive influence of the gastric and intestinal secretions by the mucus in which they are imbedded.

Tuberculosis of the *stomach* is rare, although not quite so uncommon as some authorities have asserted. In every case it is accompanied by tuberculosis of the *intestines*. The parts of the bowels most frequently affected are the lower end of the ileum and the large intestine. In the ileum the disease begins in the Peyer's patches and the solitary glands. Gray miliary tubercles form in the lymph follicles, and these turn yellow and soften from necrotic change. The mucous membrane over and adjacent to the follicles sloughs, and thus an ulcer is formed which enlarges by the additional formation of fresh tubercles round its margins and on its base. The ulcers thus spread beyond the areas of the Peyer's patches, generally in the direction of the blood vessels, and may extend around the whole circumference of the bowel. By the progressive destruction of the deeper parts, nothing of the bowel structure may be left beyond the peritoneal coat and perforation may result, but more often inflammatory adhesions are formed with neighbouring coils of intestines. Tuberculous ulcers of the ileum are not unfrequently somewhat like in appearance to typhoid lesions in the same situations. They are to be distinguished from these last by their more irregular shape, their tendency to spread across the bowel, the hardness of their base, and from the fact that very often separate tubercles can be discerned in them and on the peritoneal surface.

Similar ulcerations, commencing in the solitary glands, also occur in the *large intestine*. They form rather deep, excavated ulcers, often with a small circular opening on the mucous surface of the bowel.

The corresponding *mesenteric glands* are invariably affected along with the intestines. In some instances these glands are found in a state of caseation where there are no discoverable signs of any present or previous affection of the intestines. It is said that the disease may spread by means of the lymphatics from the mesenteric glands to those at the root of the lungs, and that thus the latter organs may be infected from a source arising from tuberculous food.

With regard to the primary infection of the glands of the neck, of the ears, the lungs, and the intestines, there is no difficulty in surmising as to the mode of access of the bacilli from the outside. Very often, however, tubercles, seemingly primary in character, are found in parts of the body remote from those last named. It may then be far from an easy matter to settle as to the manner of entrance of the organism into the body. In the vast majority of such cases careful search generally reveals an older focus of infection, most often a caseous gland. In rare instances no such source of infection is found, and in such the affection of the distant parts must be regarded as primary in character. The bacilli have here, possibly, found their way into the system from surfaces that are unaltered, as occasionally happens with small particles of foreign substances.

Tuberculosis of the *meninges* in the majority of cases is either only a part of the generalised complaint, or is secondary to disease of the ear. In a few instances it is due to a direct extension to the meninges of tuberculous disease of the brain or cerebellum. Not infrequently, however, it is apparently primary in character, no tuberculosis being found elsewhere in the body. The attending meningitis is most marked at the base of the brain, but here the resulting fibrinous effusion, matting the parts together, may be so dense as to mask the tuberculous nature of the disease. The tubercles are found in the greatest numbers in the fissure of Sylvius, vary greatly in size, and when very minute are perhaps more easily felt than seen. They apparently begin in the perivascular spaces surrounding the smaller arteries, and accompany the arterioles into the meninges and the brain substance. Along with the meningitis there is always a varying amount of cerebritis as well. In the greater number of cases of tuberculous meningitis, tubercles are present also in the choroid plexus of the ventricles.

Tuberculosis of the *brain substance* may result in the formation of caseous masses varying in size from that of a pea to that of a walnut. In the brain the individual tubercles and the masses they form are larger than in any other part of the body. In recent cases the caseous masses are apt to be surrounded at their circumferences by a layer of gray miliary tubercles. The tuberculous tumours are almost invariably multiple in number, and are most frequent in the cortices of the cerebral hemispheres, the cerebellum, and the pons, in the order given. In some cases they give rise to no symptoms at all, and are only revealed by post-mortem examination. In other cases they produce all the symptoms of cerebral and cerebellar tumours, and tubercle accounts for the larger number of growths found in these situations. In infants and young children tuberculous masses in the cerebral hemispheres are a frequent cause of a permanent hemiplegia.

Tuberculosis of the *peritoneum* may occur from the direct perforation of an ulcer of the intestine into its cavity, or as only a part in the widespread disease. Not unfrequently, however, usually in childhood, it is apparently primary in character. In its acute forms the peritoneal surfaces, both visceral and abdominal, are studded with very numerous gray miliary tubercles, and the cavity is rapidly distended with the out-poured fluid. In more chronic cases the peritoneum is greatly thickened, the intestines are densely matted together, and there is a tendency to obliteration of the peritoneal cavity.

In acute general tuberculosis the *spleen* is invariably affected, and in a large proportion of cases of the more chronic infection it is the seat of tubercle. Beyond enlargement of the organ, never of any great extent, there are no symptoms or physical signs attending tuberculous disease of the spleen.

The *liver* is affected under the same conditions and in the same proportion of cases as the spleen, and in addition tubercles on the peritoneal surface may penetrate into the substance of the organ. Tuberculosis of the intestines, too, may lead to that of the liver, owing to the virus being carried to the last by means of the mesenteric veins. In this case the distribution of the tubercles may correspond closely with that of the portal vessels. As a rule, tuberculosis of the liver is only clinically manifested by enlargement of the viscus. Tuberculosis of the portal canals, however, may give rise to an overgrowth of connective tissue, and cause one of the forms of hypertrophic cirrhosis of the liver.

Tuberculosis of the *kidney* occurs in two distinct forms. In

the general complaint gray miliary tubercles, or small caseous masses, are scattered throughout the kidneys, more especially in the cortical portions, to which the capsules are generally adherent. In the other form the lining membrane of the hilum is the seat of varying degrees of ulceration and caseation (tuberculous pyelitis), which lead on gradually to the destruction of the kidney. From the kidney the disease spreads to the ureter, which may be lined with caseous material throughout its whole course, and from the ureter the disease may spead by continuity to the bladder. The kidney is more or less enlarged in a large majority of cases of tuberculous pyelitis, and when the ureter is blocked by the caseation there may be a condition of pyo-nephrosis. Only one kidney may be affected, and when both are attacked one is generally much more affected than the other.

Tuberculosis of the *bladder* is extremely rare as a primary manifestation, and is generally secondary to tuberculosis of the testicle or the kidney.

Tuberculosis of the *testis*, apparently primary in origin, is far from uncommon. Here it attacks the epididymis, and an indolent tumour is formed which almost completely surrounds the testicle. In adults and older children the disease has a great tendency to extend by means of the spermatic channels to the vesiculæ seminales, the prostate, the bladder, and even up to the kidneys. In children under the age of seven the disease usually confines its ravages to the epididymis itself, and a chronic abscess often forms which bursts through the scrotal walls.

Next to the lymphatic glands, the *bones and joints* are the most frequent sites of the localised complaint in childhood. The spongy portions of the bones are the parts chiefly affected, and in the long bones it is the epiphyses entering into the formation of the joints that are mainly involved, leading to necrosis of the cartilages and infection of the lining membranes, along with destructive changes in the joints of a greater or less severity. In the spinal column the contiguous surfaces of adjacent vertebræ are commonly affected, and it would seem as if the disease had started in the inter-vertebral cartilaginous discs, but owing to the non-vascularity of the latter such an origin is unlikely. In the joints the complaint may start in the membranes instead of being an extension from diseases of the bones. Cases commencing in disease of the membranes are usually more chronic in their course than those beginning in disease of the bones.

It is not uncommon for cases that have for a long time been

essentially of the chronic and localised form to suddenly take on an acute and generalised character, owing to the entrance of the virus into the general blood stream. Such an occurrence is usually marked by an access of fever and bodily distress, apart from any symptoms arising from the implication of fresh organs in the complaint. The generalised form may even follow upon such purely local conditions as tuberculous disease of the bones.

The distribution of tubercle in the different organs in the generalised disease is one of scientific interest rather than one of practical importance. Many published lists differ widely in their estimation of the frequency with which the different organs are involved, and this is bound to be the case where so much depends upon the individual care and upon accuracy of observation. All statistics, however, agree upon the rarity with which the lungs escape. This is doubtless owing to the fact that in extension from most parts of the body, whether directly by the blood vessels or indirectly by means of the thoracic duct, the bacilli have to pass ultimately through the capillaries of the lungs. Out of sixty-three cases of general tuberculosis, tabulated by Dr. Shardlow at the East London Children's Hospital, in only five were the lungs recorded as free, and in two of these five the bronchial glands were caseous. Of the remaining three, in one the tubercles were almost confined to the pleura, pericardium, peritoneum, and meninges; in one the peritoneum and meninges were chiefly affected; and in one there was ulceration of the intestines, with caseation of the mesenteric glands. It is noteworthy that, in all the sixty-three cases, in one only the disease seemed to have its primary origin in the intestinal membranes. In the same cases the liver was recorded as tuberculous in thirty-one instances, or about fifty per cent. This possibly understates the percentage of cases of involvement of the liver, as in that organ the tubercles are often so microscopic in size that they are overlooked. The frequency of tuberculosis of the liver is no doubt due to the virus being carried to it from the other abdominal organs by the portal vein.

Influence of age and sex.—General tuberculosis is infinitely more common during the first two years of life, and there is a lessening tendency to it with each year of life up to the age of puberty, after which it is comparatively rare. Tuberculosis of the bones and joints, the lymphatic glands, and to a less degree the testicles, is most frequent in childhood, but is far from uncommon in adult age. Chronic pulmonary tuberculosis is uncommon under the age of seven, but the tendency to it increases with every year up to the age of puberty. It is most frequent between this last

and the age of twenty, and after this decreases with each decade of life, until it becomes comparatively rare after the age of forty as a primary complaint, and extremely so after that of sixty. Tuberculous meningitis is rare under the age of six months, and is most common between this age and that of puberty; but it is much more common in adults than is generally supposed. As a whole it may be taken that tuberculosis is commonest in childhood and early adult life, but there is hardly a single phase of it that may not occur in extreme old age.

There are no reliable statistics showing that there is any marked tendency to tuberculosis in the one sex over the other. It is the general experience that the progress of tuberculosis is frequently arrested during pregnancy, to develop with increased virulence after parturition.

Contagiousness.—There is no certain proof that tuberculosis is contagious in the ordinary sense of the term; but that one person can indirectly contract the disease from another is incontestable. From the wide prevalence of tubercle bacilli, both in the air and articles of food, it would appear that less importance should be attached to its mere presence, and more to the element of predisposition to the disease. That the members of certain families are specially prone to the disease is indubitable, but this is due, not to the direct transmission of the virus, but to a hereditary susceptibility to contract the complaint, or, more strictly speaking, to a lessened resistance to its attack. This susceptibility may not only be inherited, but acquired. It is principally acquired by those persons in whom the general health is reduced, and especially by those in whom the respiratory functions are placed at a disadvantage. Thus tuberculosis is most common amongst the inhabitants of over-crowded dwellings, in those breathing the vitiated air of factories, and in those exposed to the inhalation of finely divided dust. Chronic alcoholic excess is also an important predisposing cause. There is not only a predisposition on the part of certain individuals to acquire the complaint, but in some of these the vulnerability to the disease may rest only in particular tissues of the body. It is only by the conception that the vulnerability is restricted to certain tissues that an explanation can be found of the simultaneous affection of several of the serous membranes in the same individual, in whom the rest of the tissues escape. Again, it is not uncommon for many of the bones of the body to suffer from tuberculosis, either simultaneously or after long intervals of time, with no evidence of the disease in other parts. This susceptibility on the part of particular tissues may be inherited,

and it is not unusual for the members of certain families to die mainly from the effects of the complaint on the cerebral meninges, whilst in other families the chief stress always falls on the lungs or abdominal organs.

Curability.—Acute general tuberculosis is invariably fatal. The same fatal prognosis attaches to tuberculous meningitis, as cases of recovery are too exceptional to afford any reasonable grounds for hope when the disease is well marked and unmistakable. The majority of cases, indeed, of reported recovery from tuberculous meningitis, as Henoch has pointed out, have probably been examples of croupous pneumonia with cerebral symptoms where the diagnosis has been at fault; or of pneumococcal meningitis secondary to the lung affection. Cases of the more chronic form of general tuberculosis, even where there is evidence of many organs being involved, may undoubtedly recover temporarily, but only too often the disease recurs with a fatal termination. Still, there is no proof that all such cases relapse, and the fact that temporary recovery is possible affords reason for belief that in exceptional instances recovery may even be permanent and complete. In most other cases, except perhaps when the disease is far advanced in the lungs or intestines, tuberculosis is far from necessarily fatal, and complete recovery may occur. Very often post-mortem examinations reveal the presence of unexpected tuberculous lesions which had long been recovered from and become obsolete, and in many such cases there is no history of the patient having at any time suffered from tuberculosis. In numerous instances, too, tuberculous disease is apparently recovered from, but only to recur again shortly after the onset of more acute disease, such as one of the exanthemata. Measles, in particular, is frequently responsible for relighting up quiescent tuberculosis, and this in a manner beyond its mere power of setting up a catarrhal state in numerous regions. Some authorities, too, state that surgical operations often convert a localised tuberculosis into one of the generalised form, but the alleged frequency of this occurrence is not, perhaps, in accord with general experience.

Clinical symptoms.—In every case where there is any wide distribution of tuberculous disease fever is a marked feature of the complaint. The fever, too, is specially characterised by its irregular nature. In some cases the temperature is high in the mornings with evening remissions, and in others it is heightened in the evenings with remissions nearly to the normal in the mornings. These two types of temperature, again, may be present in the same case at

different stages of the disease. Death may ensue from the general condition, apart from any disease special to the organs involved; and here the heightened temperature may be the only prominent symptom during life. In the majority of cases, however, the fever is accompanied by profound pallor, and rapid wasting from no obvious cause.

Where death is delayed, in addition to fever and wasting, there are often symptoms arising from the implication of special organs in the complaint. Of these last, the lungs undoubtedly most often furnish evidence of being attacked. It must not be forgotten, however, that the lungs may be extensively riddled with tubercles where the physical signs are healthy both to auscultation and percussion. In other cases the only evidence of extensive involvement of the lungs may be high-pitched, somewhat metallic râles audible generally over the chest. Where the disease is of longer standing, there may be the physical signs of more or less extensive consolidation of the lungs; and it is noteworthy that such consolidation is most frequent at the bases instead of at the apices, as it is in the chronic and localised forms of the complaint. In exceptional instances signs of softening and cavitation may follow upon those of consolidation in the affected lungs.

Next to the lungs the nervous system most frequently shows signs of special implication in the disease, and many patients with general tuberculosis die with head-retraction, vomiting, and progressive coma, the results of meningitis, as the only prominent evidences of the widespread complaint.

In a minority of cases the chief stress of a general tuberculosis falls upon the abdominal organs, and the victims may die apparently from the effects of a protracted and incurable diarrhœa. In rare instances rose spots, indistinguishable from those of enteric fever, may occur upon the abdominal walls, and it has been asserted, but on no reliable grounds, that such spots in tuberculous subjects are invariably associated with disease of the intestines. The spleen is generally enlarged, and this splenic enlargement is often the earliest physical sign of general tuberculosis. In young infants, who are much wasted, hæmorrhagic staining is common upon the abdominal walls and elsewhere, but such staining may occur in wasting from other complaints besides tuberculosis, although it is, perhaps, most marked in the last.

In many cases the resemblance of the symptoms of acute general tuberculosis to those of enteric fever may be very marked, and in the early stages of the two complaints it may be extremely difficult, if not impossible, to distinguish between them. In tuber-

culosis, however, the temperature seldom assumes the regular rise and daily variations characteristic of enteric fever; the tongue, as a rule, is less furred; if diarrhœa be present the stools very seldom present the typical appearance of those that occur in enteric fever; wasting takes place earlier and is more rapid; and there is a greater tendency to early and progressive coma. All these distinctive signs, however, may fail us; and then valuable assistance may be derived from the serum test.

It must be remembered that the presence of tubercle favours invasion by staphylococci, streptococci, and other organisms, and that such mixed infection is frequently met with, contributing its own symptoms to the general morbid manifestations.

Duration.—In cases of acute general tuberculosis death is seldom protracted beyond the limits of three weeks or a month. The same time may be fixed as the limit of the course of cases of tuberculous meningitis. The duration of the less acute cases of general tuberculosis is usually to be reckoned by months rather than by years. In most other phases of the complaint the duration is dependent on so many factors that no possible general rule can be adduced. When the disease is restricted to non-vital parts death may be indefinitely postponed, and, when it occurs, is usually due to the supervention of acute tuberculosis or to the lessened resistance to other complaints induced by the original disease.

Treatment.—In the light of our present knowledge the prognosis of general tuberculosis is hopeless, and treatment is practically unavailing. The utmost that can be done in this last is to control temperature, to check convulsions and diarrhœa, and to relieve pain. The hopes founded on tuberculin a few years back proved a failure, and its use in many cases was a source of danger, if not of positive harm. A small minority of cases, however, improved temporarily under this agent in the most striking manner. It is, perhaps, in the direction of the discovery of a more perfect tuberculin, or some serum remedy, then, that hopes should rest in the future treatment of the established disease. If at present nothing can be done in the way of cure, much can be done in the way of prevention. Improved hygiene, especially the ensurance of abundance of fresh air, and the non-exposure of the predisposed to sources of infection, would guard many a one from the disease. The services of the surgeon, too, might be more often employed in the removal of scrofulous glands than is the present custom, to prevent the spread of the virus to more vital parts.

J. A. Coutts.

LEPROSY

A chronic specific disease tending to a fatal issue, the result of infection by the *bacillus lepræ;* characterised by the formation of granulomatous infiltrations of the skin and of certain nerves and viscera, which induce functional irregularities and trophic changes in the parts affected.

The names "elephantiasis græcorum" and "lepra," which have been applied to the malady, are liable to lead to confusion. The former is apt to be confounded with the filarial disease elephantiasis arabum, or true elephantiasis, and the latter is a term employed by Willan to designate a disease having nothing in common with leprosy except a cutaneous resemblance. Leucoderma, a common condition more particularly amongst the yellow races, has, owing to the Biblical phrase, "a leper as white as snow," come to be viewed with suspicion without any reason.

History.—Leprosy seems to have existed among all the ancient peoples of the earth who have recorded their histories, whether Egyptians, Jews and their neighbours, Hindoos or Chinese. It may fairly be assumed also to have existed amongst many other less literary races of the earth, from what we know of them at the present day. Although leprosy is chronic in nature, but slightly contagious, and but slowly infectious, it would seem that the tide of its intensity flows and ebbs, and that waves of the disease pass over portions of the world at long intervals. In ancient and mediæval times we find countries at one time free from leprosy being invaded and again purged of the disease. Greece, previously free, seems to have been attacked about 400 B.C., as intercourse with Egypt increased, and the Crusaders appear to have been responsible for leprosy reaching Western Europe, where, after establishing itself for some 300 or 400 years, it subsequently receded, until at the present day it is all but extinct. On the other hand, in modern times, we find leprosy reaching countries never before visited; of these the Hawaiian group of islands is the most marked example. Some fifty years ago the disease was unknown in these remote Pacific Islands, but now it is the most grievously affected part in the world.

Geographical distribution.—At the present day lepers are met with in increasing numbers as the equator is approached, and its

presence is in inverse ratio to sanitary advance. There is perhaps no country in Europe, Asia, or Africa quite free from the malady. Of European countries the British Isles contain perhaps the fewest, and Norway, in proportion to population, perhaps the greatest number of lepers. In Asia two great leprous centres exist, viz. Northern India and Southern China. Siberia, Japan, the Malay Peninsula, Cochin China, Arabia, Syria, the great islands of Java and Sumatra, and many, but by no means all, of the islands of the Eastern Archipelago are tainted. Australia has lepers within its seas, but they are for the most part Chinese, as are the majority of lepers in the Pacific Archipelago.

Africa, North, South and Central, has lepers amongst its varied peoples. In the best known parts they are fairly numerous, as Egypt in the north and as Robin Island off Cape Colony with its leper settlement testify. In the western hemisphere the same law holds good, namely, that as the equator is approached the number of lepers increases, and in tropical America and the West Indian Islands the disease is prevalent.

Etiology.—The *bacillus lepræ* is the one pathological factor in leprosy which requires to be discussed. Before its discovery in 1871 the supposed causes of leprosy were multitudinous. Amongst these, want of salt, malaria, unwholesome food, scrofula and tuberculosis, syphilis, scurvy, anæmia, etc., each had its advocates. Mr. Hutchinson's theory that the consumption of uncooked fish is the vehicle of contamination in leprosy has been neither proved nor disproved, and many arguments for and against the idea may be adduced. Heredity finds believers and disbelievers. Against the transmission of leprosy from parent to child is the fact that no child is born leprous, and that the suckling of a leprous mother does not exhibit signs of leprosy. It is seldom before the third year that a child so brought up becomes leprous, and the appearance of the symptoms may be delayed until the period of puberty. All clinical evidence points to prolonged and intimate contact as being the real channel of transmission. From husband to wife, or *vice versâ;* from one member of a family to another, more especially when sleeping together; from mother to child, especially if the child is breast fed; from the native leper to the healthy European, if occupying the same bed for a time; and by sexual intercourse, are some of the more direct means of conveying the contagium from one person to another. And yet intimate contact is not certainly provocative. The writer saw a woman, married to three leper husbands in succession, and living among lepers, in the leper village in Canton, who was perfectly

free from any leprous taint or mark. A number of such cases are on record, showing that leprosy is by no means highly contagious or infectious: in fact, many deny the propagation of leprosy by contagion at all. It would appear that leprosy is on a level, in this point, as in many others, with tuberculosis, and just as tubercle is occasionally conveyed from one person to another, so it would seem leprosy is transmissible.

Bacteriology.—The microbes of tuberculosis and leprosy are closely allied in their microscopic appearance and in their reactions to staining fluids. Specimens of the bacillus lepræ can be readily obtained during life from a leprous nodule or anæsthetic patch which has been rendered bloodless by being slowly compressed between the blades of a clamp or forceps. When the pale surface is pricked by a needle in several places, a clear lymph-like fluid freely exudes from the punctures. Specimens of the bacillus can be obtained in pus issuing from an ulcer, in the sputum when the disease affects the mouth or larynx, and Horder (*Journal of Trop. Medicine*, Oct. 1899, p. 68) has shown that the microbe is also found in the blood, where it occurs chiefly in the leucocytes but now and again in the plasma.

Post-mortem specimens of the leprosy bacillus are readily obtained from any leprous granulomatous tissue. The skin, the nerve sheaths, the lymphatic glands, the liver and spleen, are richly endowed; but in lesser luxuriance it is also present in the ganglia of the spinal cord, in the endothelium of the blood vessels, and in the liquor sanguinis or leucocytes of the blood. The bacillus has not been proved to exist in bone, muscle, cartilage, the tissues of the brain, the walls of the alimentary canal, the kidneys or urine.

The following method of staining the bacillus in the blood, recommended by Horder, gives excellent results:—After making cover-glass preparation, dry, float the specimens in cold carbol-fuchsine solution for twenty-four hours, wash, pass through 25 per cent sulphuric acid, wash again, dry and counter-stain with methylene blue.

The bacillus of tubercle and leprosy are so similar that their descriptions are well-nigh identical (see p. 220, and Plate II.). In one or two points only are they to be differentiated. (*a*) The bacillus lepræ when stained is decolorised less readily by acids; (*b*) the microbe in leprosy occurs almost wholly within the tissue cells, in marked contrast to the extra-cellular disposition of the tubercle bacillus; (*c*) the bacilli in leprosy tend to become aggregated in colonies.

The microscopic appearance of the bacilli in leprosy is typically a straight rod, but, just as in tubercle, club-shaped and branched forms are found. Until the present year no positive evidence of the sustained cultivation of the leprous bacillus has been known. Dr. Bevan-Rake and the writer both reported having obtained single cultivations on agar-agar in 1893, but Dr. Carrasquilla of Bogota asserts that he has successfully cultivated the bacillus lepræ in solidified human serum and on beef bouillon prepared according to the method of Thouiot and Masselin (*British Medical Journ.* July 1899). Dr. Carrasquilla cultivated the bacillus from serum to serum and bouillon to bouillon, pure cultures always being obtained. The same observer says that he noticed the bacillus to be mobile in two stages of its development; one form consists of long, slender bacilli moving in an undulatory manner; and the other form occurs as short, coarse, almost elliptic bodies moving in a straight line. Further, Dr. Carrasquilla believes he observed flagella proceeding from the shorter bacillus. Professor Campagna of Rome states that he has also cultivated the bacillus lepræ.

So far it has been found impossible to produce the signs of leprosy in any lower animal by inoculation.

Period of incubation.—This appears to be most variable. Symptoms would seem to have first manifested themselves in a few weeks, or it may be many years, after exposure to infection.

Symptoms.—For months or even years before leprosy declares itself the patients may suffer from general debility, febrile attacks, exhaustion after exertion, rheumatic pains in the muscles, neuralgia in certain nerve areas, epistaxis, sweatings, and marked mental depression. Occasionally there is complete absence of all premonitory symptoms.

The division of leprosy into "nodular" and "anæsthetic" is a mere clinical convenience, since in all cases of nodular leprosy there is an accompanying affection of the nerves and attendant anæsthesia. The attempt to multiply names by giving prominence to a mere sign or symptom is neither scientific nor useful; such names as "nerve leprosy, "macular leprosy," "lepra lævis," etc., are of this nature and do not assist our knowledge of the disease. For clinical convenience, however, the division into "maculo-anæsthetic" and "nodular" aids description, although these forms are liable to overlap.

I. Lepra maculo-anæsthetica. — The first characteristic symptom which appears is an erythematous or pigmented eruption

on the skin. The spots develop gradually or suddenly, accompanied by marked fever. All the spots become in time pale and anæsthetic in the centre, and possess a zone of red and blue vessels at the circumference, which is somewhat elevated. The spots vary in size from a diameter of a quarter of an inch to that of a crown piece, but after a time they may coalesce and embrace a large irregular area, the margins of which continue to extend until, it may be, the whole circumference of the limb is involved. Frequently the eruption is symmetrical, remarkably so, but this is by no means a constant feature. In the very early stages the centres of the affected areas become hyperæsthetic. The eruption may be seen first on the chest, but the limbs and face are very soon involved. The nerves along their trunks and in the area of their distribution show signs of implication in the pathological lesion. Neuritis increases as the disease advances, and in such palpable nerves as the ulnar and peroneal, where they cross the bones, they are to be felt thickened and are painful to pressure. In consequence of the neuritis, neuralgia supervenes, succeeded by anæsthesia and trophic changes in the part. Bulbous eruptions appear on the skin, the hair falls, the sweat glands become functionless, the nails become brittle, the joints of the fingers especially become swollen and tender, the tendons of the fingers and toes contract, and the muscles of the forearm, hand, legs and feet, atrophy and become paralysed. Facial paralysis may render shutting the mouth and eyelids impossible. The muscular paralysis is in no sense ataxic, as lepers can use even their damaged hands for fine work, and their power of walking, although weakened, is not affected when their eyes are closed. In time ulcers appear on the parts of the sole of the foot subjected to most pressure; the ulcers may be shallow, or may penetrate to the bones causing necrosis. In the hands also a similar condition obtains, and nothing is more common than to find a leper severely scalded in consequence of his putting his anæsthetic hand into very hot fluids. In the hands and feet the bones may atrophy, necrose, and exfoliate, so that mere stumps are left at the wrist or ankle. In this condition the patient is a piteous object, and the forlorn aspect is added to by the expressionless face, by the drooping eyelids and lower lip, the epiphora consequent upon the everted puncta, and it may be the loss of an eye from ulceration and giving way of the cornea owing to exposure of the eyeball. Towards the end smell and taste may be lost, gastric catarrh and diarrhœa are common, albuminuria may supervene, or pulmonary tuberculosis may carry off the patient.

II. Lepra tuberosa.—The exact period at which tubercular or nodular leprosy commences in any single individual is well-nigh impossible to ascertain. A few scattered nodules may exist for years, and the patient may either conceal them or be unaware of their significance. After a time, however, a fresh crop of nodules appears, and the process is repeated at longer or shorter intervals. Accompanying each eruption the patient is attacked by rigors and fever, which may reach 103° or 105° F., and last a day or two. With each fresh eruption the old nodules soften and may completely disappear.

This disappearance of old nodules with the formation of new, accompanied in every case by fever, suggests that during the process the bacilli lepræ are absorbed and re-deposited, giving rise to auto-infection. There are several arguments in favour of this assumption as to the manner of the spread of the leper bacillus or its products in the body. Leprous nodules vary in size from a grain of rice to a chestnut, or even half a fair-sized orange. They feel hard and inelastic, and attain a yellowish tint when of some standing. They are usually met with in the exposed parts of the body, viz. the face, back of hands and wrist, and the fronts of the legs, but afterwards they may appear anywhere except on the glans penis, the palms of the hands, the soles of the feet, and the scalp. The eyebrows, forehead and cheeks, early present signs of infiltration, but every part of the face may be so thickened and reddened that a "leonine" aspect ensues. The ears become thickened and discoloured; the eyelids become nodular; the eyes suffer from keratitis or iridocyclitis, resulting in loss of sight. The mucous membrane of the nose is infiltrated and leads to destruction of that part of the nose supported by cartilage. The mucous membranes of the cheek, tongue, gums, pharynx and larynx become infiltrated and nodular, leading to ulceration and possibly partial paresis of the laryngeal muscles.

The lymphatic glands in anatomical relation with the affected parts in both nodular and maculo-anæsthetic leprosy are always somewhat enlarged, although they never suppurate. The nerves in nodular leprosy, as in the maculo-anæsthetic, are subject to infiltration and neuritis, with consequent neuralgia, but this lesion develops later in the former than in the latter disease. The testicle, liver, and spleen, are always the seat of leprous infiltration in the nodular variety; the testicular tissue becoming wholly atrophied, and supplanted by fibrous material. As the disease advances nodules come and go, but the actual number increases with each attack of

fever. These eruptions and attacks of fever may supervene every few years, then every year, or several attacks may occur yearly. The nodules may, however, become stationary and ultimately burst, ulcerate, and then heal, leaving a scar. In the course of time ulceration often leads to lardaceous degeneration, or tuberculosis ensues, and is finally fatal after some eight or ten years.

The nodules of leprosy, when cut into, appear white and homogeneous, and the tissue beneath the microscope is seen to consist of round, epithelioid and spindle-shaped cells, and scattered amongst the cellular elements, connective tissue and a few blood vessels.

Diagnosis.—The nodular variety of leprosy is usually so pronounced in character that there is but little chance of any mistake arising. Large nodules, however, when few in number, are sometimes mistaken for Keloid growths, or, again, the nodules may be so small that only by microscopic examination and finding the bacillus can a decided opinion be given. The maculo-anæsthetic form of the disease in the commencing stages is more difficult to diagnose, but the early anæsthesia and the lymphatic gland enlargement are usually sufficient to determine its character. Charcot mentions and differentiates between the lesions of syringo-myelia and leprosy. As in the former there are neither maculæ, thickened nerve trunks, nor enlarged glands; there is no occasion for confusion to the careful observer. Tertiary syphilis perhaps exhibits lesions which resemble some leprous conditions more closely than any other disease. The means of diagnosis, however, is always at hand, namely, the demonstration of the lepra bacillus.

The leper is subject to many skin affections which may obscure the real disease. Scabies is a common accompaniment, but eczema, lichen, psoriasis, etc., are often met with.

Prognosis.—Leprosy is essentially a chronic disease, but occasionally, owing to rapid exhaustion of strength, some fatal intercurrent affection supervenes within a year or two. Nodular leprosy is much more acute than the maculo-anæsthetic variety; the average lifetime of the leper afflicted with the former, after the malady declares itself, is eight to ten years. But in the case of the latter, life may be prolonged for a period of fifteen to twenty or even forty years.

The patient succumbs usually to phthisis, pneumonia, nephritis, or amyloid degeneration of the viscera. So-called spontaneous cure is recorded, but it would seem to be merely a cessation of infection, the nodules disappearing to be succeeded by a scarred anæsthetic patch. "In the maculo-anæsthetic form the cure of the

leprosy is almost invariably the result" (Hausen and Looft). On excellent authority it would seem that leprosy may disappear and leave a healthy man, but the rule is that a maimed and mutilated being is left to continue a miserable existence.

Treatment.—There is no specific treatment for leprosy; many drugs have been announced as such, but a temporary reputation is all that any one of them has attained. The destruction of the bacillus, either by medicinal or hygienic treatment, is what has to be aimed it. With this intention Unna introduced pyro-gallol and chrysarobin and Dr. Danielssen the salicylates. The ointment employed by Unna for application to the body consists of:—chrysarobin, 5 per cent; salicylic acid, 2 per cent; ichthyol, 5 per cent; lard to 100. When the ointment is for the face Unna recommends pyrogallic acid, 6 parts; salicylic acid, 2 parts; ichthyol, 5 parts; lard to 100 parts. The administration of 10 drops of acid hydrochloric dil., twice or thrice daily, counteracts the deleterious action of the pyrogallic acid. The writer had very gratifying results in numbers of cases of leprosy treated in this manner. Chaulmoogra oil has attained a considerable reputation; 10 drops and upwards are given in milk twice daily; and externally it is applied with olive oil (1 in 16) as an embrocation, which is allowed to remain on the skin for some hours and then washed off with soap and water. Gurjon oil has been employed in a similar manner.

Dr. Danielssen's treatment is perhaps the most satisfactory. The general health of the patient is first improved by good food, and the administration of cod-liver oil, iron and quinine. When the general condition is fairly good 15 grains of salicylate of soda is administered three or four times a day. The dose may be gradually increased, and its use continued for six or twelve months.

The writer has employed almost every drug recommended for leprosy by the Chinese, but with no marked benefit; and besides these creasote, phosphorus, arsenic, mercury, aristol, naphthol, and salol, etc., with similar unsatisfactory effects.

Koch's tuberculin was first tried by the writer on an extensive scale, as many as fifteen lepers being under treatment at a time. A certain number responded to the treatment, but in a few no effect was produced. In some the effect was most marked, almost all cutaneous signs of leprosy disappearing after the initial fever had subsided. In several cases coolies who suffered from leprosy, and who had been driven off by their fellow-labourers from working alongside of them were, after treatment by tuberculin, received back

amongst them as "cured." Unfortunately the beneficial effects were transitory.

A curative serum has been prepared and employed, but, so far, with dubious results.

Surgically the leper may require:—to have tracheotomy performed; operations for ectropion, iridectomy, etc.; removal of dead bone when the bones of the hands and feet necrose; nerve stretching in cases of anæsthesia, etc. When the nerve trunk supplying a paralysed area is stretched and incised longitudinally, the sensation may return and the muscular power reappear for a time.

Prophylaxis.—Complete segregation of lepers with separation of the sexes is the only known system whereby the spread of leprosy may be held in check.

James Cantlie.

MYCOSES

In addition to animal and bacterial parasites the human body is liable to be attacked by a number of vegetable parasites, and more especially by certain fungi; and although, strictly speaking, bacteria belong to the vegetable kingdom, it is convenient to distinguish the diseases due to bacterial invasion from those dependent on the parasitic activity of fungi and other similar organisms.

The number of fungi that are found either associated with or actually causative of pathological lesions in man is daily increasing. It has long been known that certain skin diseases are dependent on the presence of these organisms, but it is only comparatively recently that other diseases have been found to be associated with or dependent on the presence of such vegetable parasites as the fungi.

The most important of these maladies are those known as actinomycosis and aspergillar mycosis, but it is convenient to give the name of mycosis to the entire group, including under this such diverse affections as various forms of dermatitis, otitis media, and possibly certain tumours.

Various species of *Blastomycetes* (saccharomyces) have been found associated with a number of inflammatory states usually chronic in character, such as otitis, less often running a definite pyæmic course. Further, these fungi have been found in other conditions besides inflammation. Thus a cystic growth of the tibia has been recorded

where the broken-down material in the cyst contained a large number of saccharomyces, and in this case a general pyæmic infection occurred and the metastatic foci contained the same organism.

Several observers have described the presence of yeast-like organisms (blastomycetes) in malignant growths, both sarcomatous and carcinomatous. In many of the cases of inflammatory lesions, and perhaps in some of the malignant cases, the presence of the fungus may be due to accidental causes and to secondary infection, the fungus being a saprophyte and not the cause of the lesion. In others, however, it is apparently definitely parasitic and pathogenetic, since the inoculation of animals with a culture of the fungus has led to the formation of similar lesions to those occurring in the human subject. In addition to various species of blastomycetes, *Mucor*, *Penicillium*, *Aspergillus*, and other fungi have been found associated with a variety of pathological states, both in the human subject and in warm-blooded animals. The spores of *Penicillium*, when injected experimentally into animals, cause not only emboli, but a mycelium is under certain circumstances produced, which extends inside the vessels and passes through their walls into the adjacent tissues, and its presence here is asserted to cause a fatty and granular degeneration of the tissues, and death may result.

The infection caused by some of these fungi, and more especially that produced by actinomyces and aspergillus, is characterised by the formation of granulomata which resemble superficially those produced by the virus of syphilis, or tubercle, or glanders; the last two disorders at any rate are definitely proved to be of microbic origin, and thus the lesion produced by the fungi resembles that produced by certain microbes; but whereas the microbes produce, in addition to granulomata, toxins which often exert a poisonous effect on the body at large, the fungi apparently produce all their pathological effects either mechanically or by interfering with the oxidation of the tissues, and there is no evidence either in the case of actinomycosis or of aspergillar mycosis of the production of any toxin.

The most important mycoses clinically are actinomycosis, madura foot and aspergillar mycosis.

Actinomycosis

Actinomycosis is an infectious malady characterised by the formation of granulomata, affecting man and many domestic

animals, and is dependent on the growth of an organism belonging to the genus *Oospora* according to some authors, but it is more usually described as a species of *Streptothrix*. The disease is more especially prevalent in cattle, the jaws and tongue being the parts most frequently affected, but it is also found widely disseminated in the internal organs. It is rare in horses and donkeys, and occurs occasionally in the pig and sheep. In some herds of cattle it has been observed to the extent of 8 per cent, and it is said to be especially prevalent in the fen country.

In the human subject from 50 to 80 per cent of the cases attack primarily the cervico-facial region, including the mouth. The abdomen and chest are next most frequently affected, and the skin and limbs are the least often involved.

Histology.—The actinomyces occur in the form of yellowish-green grains, the largest of which are the size of a pin's head, and of rather irregular oval or reniform outline. These are found in the depths of the tissue affected and also in the pus. Each grain consists of a central portion composed of a mycelium, and at the periphery are found the characteristic clubs arranged more or less irregularly. In addition to these, spores of 1 to 2 μ are scattered through both the central and peripheral portions of the granules, but most abundantly in the former situation. The most constant structure in the actinomycotic granule is the mycelium (Plate I.). This consists of threads of from 1 to 2 μ in breadth, and varying from 3 to 100 μ in length. The growth of the organism occurs by the formation of spores, and these spores are developed from certain filaments which are rather thicker and more differentiated than the neighbouring ones. It was formerly thought that the clubs were also concerned in the process of reproduction, but more recently it has been demonstrated that the club formation depends on hyaline degeneration of the peripheral portion of the filament constituting a kind of sheath. The cultivation of actinomyces is difficult, but it can be grown in peptonised broth and on agar, and it develops readily on the moist surfaces of cereals at a temperature of 35° to 37° C. Inoculated into animals it grows with facility in the peritoneal cavity of the rabbit, but it is difficult to obtain virulent cultures.

Mode of infection.—The malady has been communicated to man by contact with animals affected, but this is rare, and it is seldom one infected animal conveys the disease to another. It is more usual for the human subject to become infected through barley and rye, both of which are frequently affected with the fungus. Infection is probably caused by chewing the fresh grains, which have

been actually found in the seat of the lesion. The presence of carious teeth is undoubtedly an important predisposing cause. Cereals are not the only materials by which the disease is communicated, and numerous instances have occurred where the disease has developed as the sequel to a wound produced by a splinter of wood, but the infecting agent usually enters the body either through the digestive tube or the respiratory tract.

Course and symptoms.—Clinically the disease presents itself in two forms. In the one the lesion simulates to a greater or less extent a new growth; in the other it is more definitely inflammatory, and leads to suppuration, but even in the latter case the abscesses formed are characteristic in being surrounded by extensive chronic inflammation and induration, so that they have exceedingly thick walls. The likeness to a new growth is owing to the fact that the actinomycotic tumours are granulomata, and the resemblance is especially great when the face and jaws are attacked and the malady has existed for some time. The differential diagnosis from malignant disease is difficult in the early stages. After a time, however, portions of the growth break down into pus, and this ultimately reaches the surface through long fistulous channels. A very characteristic appearance is for one side of the face and neck to be occupied by a tense brawny swelling, covered with livid and congested skin, in which are several ulcerated sinuses discharging pus. The association of the mass with a purulent discharge is very characteristic. Similar tumours not uncommonly involve the jaws, the floor of the mouth or the tongue, and in all cases they have the characteristics described above. It is probably impossible to diagnose the disease until a certain amount of breaking down has occurred. The pus, usually inodorous, often contains the yellowish-green grains characteristic of actinomyces, which somewhat resemble particles of iodoform, and are easily visible to the naked eye. In the abdomen the liver is most frequently the seat of the deposit of actinomyces, and the appearance produced here is also very characteristic. The organ may be greatly enlarged and contain a mass the size of a fœtal head or even bigger. On section the tumour is yellow or greenish yellow in colour, and has frequently a peculiar arborescent appearance, especially in the more peripheral portion of the growth, the structure consisting of a dense fibrous framework, the meshes of which are occupied by softer purulent material, which can be washed away. Occasionally there are multiple foci and still more frequently the disease spreads from the liver through the diaphragm into the lung, as the mode of growth is almost always by

continuity. Actinomycotic tumours thus resemble aneurism in their mode of extension, involving and destroying all the tissues without any regard to anatomical limitations. Sometimes the growth spreads so as to involve the abdominal and costal parietes, and ultimately reaches the surface, a long fistulous and sinuous track surrounded by dense fibrous tissue, discharging externally the pus which may be formed at a great depth in the liver, lung, or other viscus. It is probable that in all cases of apparent primary actinomycosis of the liver that the real primary seat of the mischief has been in the appendix, or some other portion of the alimentary canal. Actinomycotic deposits in the right iliac fossa in connection with the appendix are not uncommon, undoubtedly occurring more frequently than is supposed, inasmuch as the diagnosis is difficult, unless the pus is examined microscopically. Occasionally cases have been recognised by the microscopical examination of the fæces, the characteristic grains have been found, and have at once cleared up the nature of the hard dense tumour-like mass occupying the iliac fossa. In these cases of actinomycotic appendicitis there is usually great induration, so that the pus may only be reached by incising a mass of fibrous tissue perhaps an inch thick, and it is for this reason that the lesion in this neighbourhood is peculiarly apt to be mistaken for malignant disease.

Actinomycosis of the lung may be primary, in which case the causal organism is supposed to have been inhaled, or it may extend from some neighbouring part, as the œsophagus or liver or even the root of the neck; or the lung may contain numerous metastatic deposits reaching it through the blood from some primary mass elsewhere. Some cases have been described where the lungs were studded with minute nodules simulating those of tubercle; more frequently, however, the disease in the lung leads to the formation of a tumour-like mass, in which a cavity or cavities containing pultaceous puriform material are found; these are surrounded by dense fibrous tissue which spreads irregularly through the lung, and so produces an appearance very similar to that seen in some forms of malignant growth. The bases are more liable to be affected than the apices. It may lead to the production of pleurisy or of empyema, or may even spread and involve the chest wall and discharge externally much in the same way as in hepatic actinomycosis.

In the case of the skin, growths simulating sarcomata in their softness and their general appearance are produced, but very soon ulceration of the integument occurs with the formation of crater-like ulcers discharging the characteristic pus.

Lymphatic glands are not commonly affected in actinomycosis, the virus being disseminated more usually through the blood stream, and even when the disease has produced a large mass breaking down and ulcerating in places, it is exceptional to detect clinically any marked glandular enlargement.

The general symptoms include more especially fever and wasting. Mechanical effects dependent upon the anatomical position of the lesion are necessarily present in many cases. Cough, in the pulmonary form of the disease, is a prominent symptom, more especially in the "bronchitic" type of the malady. The fever is, as a rule, moderate in its intensity, rarely exceeding 103°, and more usually not rising above 101°. The course of the fever is very similar to that seen in chronic suppuration. The disease is usually chronic. It may, however, run an acute course, more especially when complicated by secondary affections.

Diagnosis.—When a tumour is produced which can be felt the principal error that is made is to confound it with a malignant growth such as a sarcoma. When the growth has caused ulceration, as, for instance, in the neck or in the tongue, it is liable to be confounded with epithelioma. The occupation of the patient rendering him liable to infection, and more especially the examination of the pus, will throw light on the nature of these cases, which are, however, always obscure.

In visceral actinomycosis the diagnosis is still more difficult, unless a sinus has formed, owing to the disease having spread to the surface of the body; usually the case will only be recognised during an operation, unless the characteristic grains have been found in a discharge or in the fæces. The case will probably be looked upon as one of malignant disease, or perhaps as one of abscess.

In the case of pulmonary actinomycosis it is most apt to be confounded with tuberculosis, since it so frequently produces a persistent bronchitis and recurrent pleurisy and effusion, and here also the diagnosis can only be made in the earlier stages by a microscopic examination of the expectoration. In the fully established and later stages of the disease the characteristic involvement of the chest wall and the formation of sinuses will reveal the nature of the case.

Treatment.—Some forms of actinomycosis, as for instance the cervico-facial, the buccal, and actinomycotic appendicitis, are fairly amenable to surgical interference; this is more difficult, but not impossible, where the malady is deep-seated in the lungs or liver. The

hæmorrhage from scraping actinomycotic sinuses is, however, sometimes very excessive.

Pulmonary and visceral actinomycosis are often beyond the reach of surgery, and are most suitably treated by the administration of iodide of potassium, which has a very great influence on the malady both in man and in animals. Large doses, 20 to 30 grains three times a day, are necessary, and this drug is also of considerable value in the treatment of the other forms of the disease involving the face, skin, neck, and tongue. Different observers estimate the value of this drug differently, but it seems certain that only a small proportion of cases are really cured by its administration even in large doses. Tonics and a liberal diet are necessary to counteract the general weakness.

When the disease involves the skin and subcutaneous tissues the local treatment should consist in the application of some antiseptic ointment or dressing, such as boracic ointment, cyanide gauze, or boracic lint, preceded by thorough scraping, and sometimes with advantage chloride of zinc may also be used. Iodoform should not be employed.

Mycetoma or madura foot is an affection of the subcutaneous structures of the foot, very similar to that produced by actinomyces, and the resemblance between the lesions seen in the cervico-facial form of actinomyces and Madura foot is very close. The same brawny swelling with fistulous sinuses and projecting fungoid granulation tissue are seen in both conditions. The tissues of the foot are infiltrated with a mycelium which is now recognised as the cause of the disease. The mycelium of Madura foot resembles that of actinomyces, but the spores seen in the latter have not been detected as yet in the former. Two varieties of the disease are recognised, one where the infiltrated tissues are pigmented, the so-called melanoid form; the other where the lesion is colourless. The black pigmentation is usually regarded as dependent upon degeneration of the fungus. Some observers have thought that two distinct varieties of fungus, one black and one white, exist. The disease is more especially prevalent in India, and is probably dependent upon direct infection of the naked foot.

Aspergillar Mycosis

The aspergillus has been found in a considerable number of different lesions; most frequently the association of this organism

with the disease is accidental, but in some cases it is undoubtedly pathogenic and the actual cause of the conditions found after death. *Aspergillus fumigatus* is the species that is most often parasitic in addition to being saprophytic, and this is apparently dependent upon the fact that the spores of this species develop readily at the body temperature of most warm-blooded animals. Aspergillus fumigatus and A. flavescens develop readily at a temperature of 37° C. According to Lichtheim, aspergillus fumigatus has a special affinity for the membranous labyrinth, but the characteristic lesions produced by this fungus are also found in such internal organs as the kidneys, lungs, Peyer's patches, glands, etc., when the spores are injected into the circulation of animals. Primary aspergillar mycosis in internal organs removed from direct access of the air is, according to De Bary, of doubtful occurrence.

In the human subject aspergillar mycosis is most often found associated with otitis media, with a mycosis involving the nails, and in an interesting form involving the lungs, and known as pneumomycosis, usually as a purely secondary phenomenon and not as the cause of the lesions. The aspergillar infection may occur in any case of chronic otitis and frequently gives rise to no symptoms. Occasionally the fungus growth occurs primarily on the cornea or conjunctiva, and here the resulting lesion is usually of traumatic origin; thus one case is quoted where the growth followed a blow on the eye from a falling pear, and in another case from a piece of straw injuring the cornea. An ulcer of the cornea may be produced in this way in the human subject, and experimentally similar ulcers have been produced in rabbits by inoculations of the cornea with aspergillus fumigatus. It has also been found in the nasal fossæ and in the antrum. In the lungs the parasite is usually saprophytic, forming a felt-like membrane in cavities that owe their origin to other causes, such as tuberculosis or bronchiectasis, but exceptionally it is found in lungs presenting no such lesions, and in one remarkable case no other lesion was found except extreme emphysema. In this case, which occurred in a young agricultural labourer aged twenty-two and was fatal, there was reason to believe that the aspergillar growth might have produced such alterations in the lungs as to destroy their elasticity and to cause the emphysema. Clinically the case was remarkable owing to attacks of suffocative dyspnœa. Chantemesse and others have described a malady seen in France amongst those rearing and feeding pigeons which resembles chronic phthisis and is no doubt confounded with it; the prognosis, however, of the aspergillar infection is not so serious as that of the tuberculous. It

is known that recovery is not uncommon in the experimental pneumomycosis that can be produced by the injection of the spores of aspergillus fumigatus, and it is probable that similar recoveries are not uncommon in the human subject.

The diagnosis in the human subject of aspergillar pneumomycosis can only be arrived at by considering (1) the occupation of the patient, the infection usually being dependent upon the habit of chewing grain, and such grain may be infected with the aspergillus; (2) the detection in the sputum of the mycelium, hyphæ and spores; the spores can only be identified by their cultivation and by the results seen to follow their injection into animals. The pigeon is an animal very susceptible to aspergillar mycosis and usually dies some three to four days after the injection; the rabbit usually survives longer, the average duration of life being six to eight days. In the case of the pigeon the characteristic lesions are found in the lungs and respiratory tract, also in the air sacs and in the hollow bones in connection with the bronchi. Aspergillus (especially when injected into the circulation) forms little white nodules resembling those seen in tuberculosis, and this has led some pathologists to describe the lesions under the general name of pseudo-tuberculosis. In the nodules the mycelial filaments are arranged more or less radially; sometimes they assume a fan-like form. The mycelium is surrounded by macrophages and each nodule lies embedded in a necrotic area that merges into an inflammatory zone. These are well seen when the nodules are present in the lungs. The vessels are thrombosed, and, as mentioned above, the mycelium may be found in the lumen of the vessels.

For examining specimens histologically for the presence of this fungus, logwood is, according to Boyce, the most useful stain.

John Rose Bradford.

TYPHUS FEVER

A highly contagious fever, usually lasting about a fortnight, and terminating by crisis. It is characterised by sudden onset, often severe nervous symptoms, as delirium and stupor, and the presence of a mottled measly rash appearing between the fourth and seventh days, which often becomes petechial.

The bacteriology of typhus requires further investigation, and the specific microbe of the disease has not yet been certainly determined. Dubief describes a diplococcus which he terms the *Diplococcus exanthematicus.* Lewaschew, a micrococcus which in one stage of its development is flagellated, and also forms free filaments or spirochætæ: to this organism he gives the name *Spirochæta exanthematica.* Other microbes have also been described.

Etiology.—Typhus is a fever which spreads by direct contagion from the sick to the healthy, and by means of fomites, *i.e.* articles which have been in contact with the patient and to which the poison adheres. The poison appears to be given off in the breath and exhaled from the body, and where many patients are crowded together in ill-ventilated rooms it acquires intense virulence, but free ventilation renders it inert, and in a well-ventilated room very close contact is necessary to contract the disease. The corpse retains infective powers till decomposition has set in, and the disease has often been communicated to persons making post-mortem examinations or dissections. It is a disease of temperate climates, and is most prevalent during the cold season.

The predisposing causes are especially overcrowding and destitution. It invades the overcrowded districts of large towns, prisons, barracks, camps, ships, besieged cities, and is especially prevalent in times of war and famine. In the last century it was often termed jail fever, and so late as 1893 an outbreak took place in overcrowded prisons in France.

In this country it has for many years past shown a steady decline, and the same is the case in Ireland, where it used to cause great ravages. In London it is now rarely present, but it still lingers in some of the large northern towns.

Typhus is seldom seen except among the poor and miserable, and those persons whose avocations bring them into close contact

with them. In this respect it offers a marked contrast to typhoid fever.

It attacks persons of all ages, but is much less severe and fatal in the young. Under twenty the rate of mortality is very low, not above three or four per cent. Above middle age more than half the persons attacked die. It occurs equally in both sexes. One attack protects against a second, but not invariably.

Morbid anatomy.—Typhus does not cause any distinctive lesions, so that from a post-mortem examination alone it would often be impossible to diagnose the disease.

The rigor mortis is of short duration. The skin presents livid patches and petechial spots. The blood is dark and coagulates imperfectly. The muscles show Zenker's degeneration, as in typhoid. The spleen is usually, but not always, enlarged and softened. The heart is often softened, and the muscular fibres granular. There is cloudy swelling of the liver, kidneys, and other glandular organs. Sometimes there is catarrhal or even membranous laryngitis. The lungs are usually in a state of hypostatic congestion. There are no characteristic lesions of the intestinal canal, or of the central nervous system.

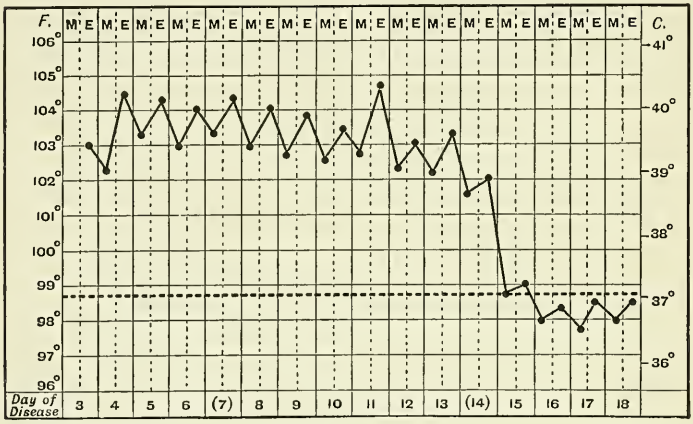
Incubation period.—The usual incubation period of typhus is about twelve days, but much shorter periods, especially when the poison has been very concentrated, have been observed, even a few hours, and it may be as long as twenty-one days.

Symptoms and course.—The onset of typhus is generally sudden. There are rigors or repeated attacks of chilliness, frontal headache, which is often very severe, pains in the back and limbs, particularly in the thighs. Feelings of weariness and prostration; sometimes, especially in children, there is vomiting. There is complete loss of appetite and much thirst. The tongue is large, pale, coated with a white fur, which soon becomes yellowish-brown. The face is flushed and dusky. The countenance dull and heavy. The sclerotics injected, eyes watery, pupils small. Pulse accelerated, full and soft. There are noises in the ears, sleep is disturbed by bad dreams. After three or four days there is often slight delirium on waking. There is rapidly increasing muscular debility, tremors, tottering gait, so that the patient usually takes to his bed on the second or third day of his illness. The temperature rises rapidly, and may attain 104 the first night. It usually reaches its maximum by the fourth night, when it may be 106; it is of a less remittent type than in typhoid, the difference between the morning and evening not exceeding one to half a degree. The bowels are

generally constipated, the urine scanty, high coloured, of high specific gravity, the urea and uric acid in excess, and the chlorides diminished ; in the later stages albumin is often present.

Between the fourth and seventh days, usually on the fourth or fifth, the characteristic *eruption* of typhus makes its appearance. It consists of two elements—a diffused dusky sub-cuticular mottling, and maculæ. These consist at first of slightly elevated spots of irregular shape and size of a rose or dusky pink colour, which soon gets darker, and in the later stages of the fever they often become the seats of hæmorrhage, and are converted into petechiæ. The

Temperature Curve in a Case of Typhus Fever.



combination of mottling and maculæ gives the rash a measly appearance. The spots usually come out first on the anterior fold of the axilla, and on the sides of the chest and abdomen, thence they spread over the trunk and limbs, but seldom appear on the face. Sometimes they are first observed on the backs of the hands, where they are commonly very abundant. At first they disappear on pressure, later they are permanent, and persist till the crisis, and do not, as in typhoid, come out in successive crops. The rash is always present, except perhaps in the very mild cases, and its amount is some indication of the severity of the attack. It is usually much slighter and more evanescent in children.

About the end of the first week the headache usually subsides ; and now, in severe cases, delirium becomes a prominent symptom.

Sometimes it is noisy and violent; the patient shouts and struggles, will get out of bed and rush about, and may even jump out of the window. This violent delirium is usually followed by great depression. More often the delirium is of a quieter character, and consists in an incoherent muttering. Both forms are attended by sleeplessness. The prostration increases, the tongue becomes dry and brown, the teeth are covered by sordes, an unpleasant effluvium is emitted from the body, and in the breath. The eruption becomes darker, and about the eighth or tenth day petechiæ begin to appear. The temperature, except in very severe cases, usually falls somewhat about the eighth day, and has a lower range during the second than during the first week. Towards the middle of the second week the symptoms of excitement are followed by nervous depression and stupor. The prostration becomes extreme; the patient lies on his back with a tendency to sink down in the bed; he is deaf, takes no notice of anything, and can with difficulty be roused; but he is not asleep, the eyes remaining half open, and he often mutters incoherently; this state, when well marked, is often termed coma-vigil; frequently there is subsultus tendinum or floccitatio. The pulse may vary from 100 to 130, and is weak and undulating; the heart's impulse is feeble, and the first sound diminished in intensity. The breathing is accelerated and shallow, and crepitant râles are audible over the back. The urine is often passed in the bed, or may be retained; it frequently contains albumin. Bed-sores are liable to form. The patient may pass several hours or days in this state; then if he survives, usually on the fourteenth day—sometimes a day or two earlier or later—a sudden improvement manifests itself. The temperature rapidly falls, often 4 to 6 degrees in the course of a single night; he falls asleep and awakes free from delirium and stupor, with his tongue moist, his skin perspiring, and an inclination for food, though he is still in a state of great prostration, from which he now rapidly recovers. Sometimes, though the crisis takes place, and the temperature falls, the patient does not rally, but sinks into a state of profound collapse, and so dies, the temperature rising again before death. In other cases the patient dies in a state of coma about the fourteenth or fifteenth day, the temperature often rising to a great height—106 or more—before death. In mild cases, where the nervous symptoms are but slightly marked, the crisis often takes place on the twelfth day, or earlier. If the fever continues after the twenty-first day, it is always due to the presence of some complication.

Varieties of typhus.—Typhus differs greatly in its severity, and extreme forms have been classed as varieties. In severe

epidemics, especially in times of war, in camps and besieged cities, the disease may be fatal in the course of one or two days. This has been termed *typhus siderans, or blasting typhus*. Very mild cases are often termed febricula. Sometimes the disease takes a hæmorrhagic form.

Complications and sequelæ.—Bronchitis, hypostatic congestion of the lungs, and lobular pneumonia, are frequently present. Sometimes there are embolic infarcts from thrombi in the heart or veins; these may soften down, or even cause gangrene. Thrombosis of the veins in the lower extremities is very common. Sometimes there is a tendency to gangrene of the extremities, probably due to arterial occlusion, either by thrombosis or embolism. Gangrenous bed-sores are liable to form. Suppurative parotitis is more common than in typhoid. Secondary abscesses are liable to form in other parts.

Meningitis is a rare complication, but sometimes occurs: and typhus may be followed by hemiplegia or other forms of paralysis, probably the result of embolism or thrombosis. Mania, melancholia, and dementia occasionally supervene, as in typhoid.

In pregnancy, miscarriage often takes place, but by no means invariably; if near the full time, the child is usually born alive, and is healthy.

Relapse in typhus, though not unknown, is of great rarity.

Diagnosis.—Typhus usually occurs in epidemics, and then can generally be diagnosed without much difficulty, but sporadic cases, and the earlier cases of an outbreak often escape recognition. The only characteristic symptom is the eruption, but this may be simulated by other conditions, or may be only slightly marked.

From typhoid the main points of distinction are the more sudden onset, the higher range of temperature during the first few days, its less remittent type, the dull heavy aspect, the injected sclerotics, the contracted pupils, the paler tongue, the absence of abdominal distension and diarrhœa, the greater tendency to delirium and stupor. The rash differs in its earlier appearance and the accompanying general mottling; the more extensive distribution, the darker colour and irregular size of the maculæ, their persistence, and their conversion into petechiæ. But nevertheless, acute forms of typhoid with a very abundant rash may be very difficult at first to distinguish from typhus. Widal's serum reaction does not seem to be a decisive criterion, as the serum in typhus appears to have some power in causing clumping of typhoid bacilli, though it acts more slowly.

The purpuric spots which sometimes occur in ulcerative endocarditis have been mistaken for the typhus rash. Rheumatic purpura may cause difficulty, the severe pains in the limbs often present in typhus may likewise simulate rheumatism, but they are muscular rather than arthritic.

The rash of measles has some resemblance to that of typhus, but the spots are larger, more raised, appear first on the face, and the other symptoms are different. Drug rashes, as copaiba, are hardly likely to cause much difficulty if care be taken.

More perplexing are sometimes cases where tramps and vagrants are attacked by some acute febrile disease as pneumonia; their skin is often discoloured by dirt and neglect, irritated by lice, and studded with petechiæ due to flea bites. These, however, are smaller than the typhus petechiæ, and the minute puncture can usually be distinguished.

Other febrile diseases accompanied by delirium, stupor, and prostration may be confounded with typhus. Asthenic forms of pneumonia and broncho-pneumonia have often given rise to confusion in both directions, the earlier causes of an outbreak having on more than one occasion been regarded as bronchitis and broncho-pneumonia. The presence of the rash and the physical signs must be the criteria.

During epidemics, meningitis, delirium tremens, and uræmia are liable to be regarded as typhus. Besides the absence of the rash which is the most important distinction, the headache of meningitis is more intense, of a more darting character, accompanied by great intolerance of light and sound (while in typhus the senses are usually obtuse), vomiting is more frequent, spasmodic and paralytic affections of the cerebral nerves are more likely to take place, and the pulse is often slow. In delirium tremens the tongue is usually moist, the skin often perspiring, there have been no rigors or severe headache, and unless there be some complication as pneumonia the temperature is not much raised. Uræmia may closely resemble typhus, the dry brown tongue, the stupor, the muttering delirium, the albuminuria are common to both, but in uræmia there is no rash, and the temperature is seldom much raised.

Treatment.—Preventive treatment requires the clearing out and disinfection of overcrowded houses, and the removal of the sick to well-ventilated rooms. All fomites should be disinfected by baking, fumigation, or steeping in disinfecting solutions. No one but the necessary attendants should be allowed access to the patients. The nurses should, if possible, be selected from those who are

rendered immune by a previous attack; where this is impracticable they should be as young as possible, as the disease is much milder in the young. The medical attendant should wear a special coat or overwrap when visiting the cases. He should never stoop down and put his ear to the patient's chest, but use a long binaural stethescope, and should avoid inhaling the air evolved when the bed-clothes are turned back.

It is of the utmost importance that the room should be cool and thoroughly well ventilated, not only for the sake of the attendants, but also for the patient's own. In a recent outbreak of typhus in a prison in Paris the earlier cases all died, the remainder were transferred to the garden and treated in the open air, and all recovered.

The general regimen and diet must be the same as that recommended for typhoid, but as there are no intestinal lesions the restrictions need be less severe, and solid food may be given as soon as the appetite returns. Alcoholic stimulants are seldom required under the age of twenty, in older patients they must be freely administered when signs of nervous or cardiac prostration appear. The temperature should be kept down by tepid bathing, sponging, cold packing, the application of cold to the head. These measures will tend to prevent or relieve the delirium and stupor. If there is great sleeplessness, some hypnotic is indicated. It is safer not to give chloral in the later stages of the fever when the heart is weakened. Opium may be given alone, or combined with digitalis; Graves strongly recommended a combination of opium and antimony; tinct. opii ℥i. ant. tart. gr. iv. aq. camph. ad. ℥ viii., a tablespoonful every two hours till sleep is induced. Where opium is contra-indicated, as where there is much hypostatic congestion of the lungs, belladonna may be given, or a hypodermic injection of hyoscin, gr. $\frac{1}{200}$.

When there is much subsultus tendinum, and floccitatio, and other signs of great nervous prostration, camphor gr. iv. and musk gr. x. used formerly to be given, and apparently with much benefit. In collapse, ether ℥ss. and liq. strychn 1 to 3 minims may be injected hypodermically. Hypostatic congestion of the lungs and lobular pneumonia require free stimulation, and ol. terebinth. m. x. combined with ether and ammonia may be administered. Counter-irritation in the form of mustard poultices or turpentine stupes may be used, but the skin must never be blistered.

The state of the bladder must be carefully attended to; bed sores must be prevented by cleanliness, the skin may be washed

with a spirit lotion, if any redness appears it may be painted with flexile collodion. A water pillow or water mattress may be employed. Secondary suppurations and gangrene must be treated in accordance with the rules of surgery.

When the patient is convalescent he should not be allowed to mix with other people in the clothes he was wearing when attacked, without their having been thoroughly disinfected, though it is best to have them destroyed; and he is to be regarded as capable of communicating the disease to others for a period of four weeks from the commencement of his illness. He himself should have several disinfecting baths. Neglect of these precautions has often spread the disease.

W. Cayley.

MEASLES

Syn. Morbilli

Measles is a specific infectious fever, characterised by catarrhal inflammation of the nasal and respiratory mucous membranes, and the presence of a distinctive red eruption.

Etiology.—The disease is met with pretty well all over the world, and is apparently independent of climate, being found to prevail under opposite extremes of temperature. Having once obtained a footing in a country, it never seems to entirely die out, though its prevalence shows considerable seasonal fluctuation. In Great Britain the seasonal prevalence of measles is peculiar, inasmuch as the monthly curve shows a double rise, one occurring in the spring and early summer, and the other in the winter, the maxima being reached in June and December respectively. Periods characterised by increased prevalence of measles have been noticed to recur every eighteen months or two years, and, according to Whitelegge, there are indications of what may be regarded as a major curve, the maxima of which are separated by intervals of about ten years.

Although the large majority of attacks are mild, the disease is liable to take a severe form in young children, especially under the influence of poverty and a defective hygiene, but no outbreak of measles comparable in severity with the form recognised in the past by the name "Black Measles" is ever met with in this country at the present day.

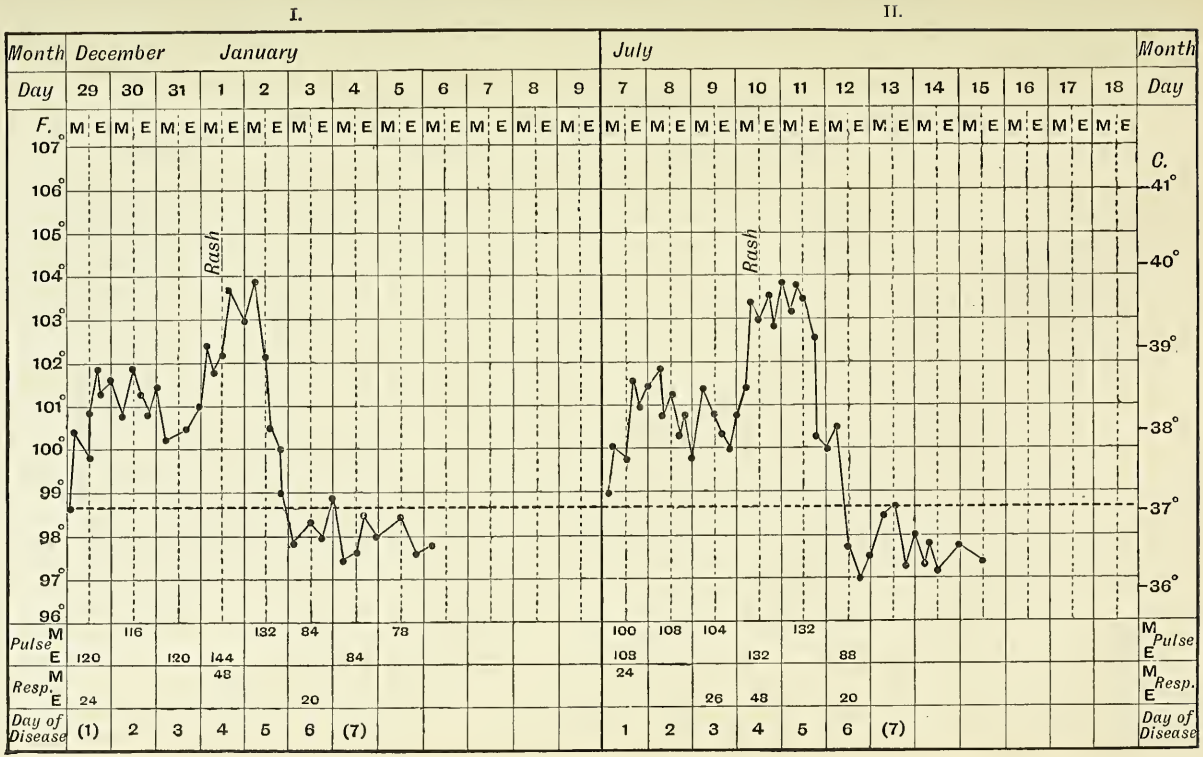
Infection in measles is usually derived from personal contact with a previous case. Indirect infection through the agency of clothes, books, toys, etc., no doubt occurs sometimes, but the activity of the contagium is rapidly destroyed by free exposure to air and light. The disease is infectious from a very early stage, even before the initial symptoms are sufficiently pronounced to lead to its recognition; hence it is that isolation of the patient, even when practised early in the attack, is so often ineffectual in checking the spread of the disease. A patient should be regarded as probably infectious for at least a fortnight after the appearance of the rash, and should not be allowed to mix with other children even then, should any sign of catarrh or desquamation be detected. School attendance is without doubt the most potent factor in the propagation of the disease.

A distinct predisposition is conferred by the presence of any catarrhal condition of the respiratory passages, so that rickety children, and those of a tuberculous constitution, are very liable to attack; and pre-eminently those who at the time are suffering from chronic bronchitis, whooping-cough, broncho-pneumonia, or actual phthisis, or who have recently had an attack of scarlet fever or diphtheria. In countries not previously invaded by the disease no special liability is apparent in respect to either age or sex. Second attacks of measles occur not unfrequently, but a true relapse is extremely rare.

The **incubation stage** in most cases of measles is about ten days; in other words, the eruption is very likely to declare itself on the fourteenth day after infection has been received. In some instances the latent period appears to be two or three days longer, and it may be shortened to the same extent. Sixteen days should elapse after a child has been exposed to infection before it can be regarded as free from the suspicion of having taken measles, disinfection having been carried out at the commencement of the quarantine.

Symptoms.—The invasion is characterised by the sudden access of fever and more or less catarrh. The temperature may reach 103° F. by the evening of the first day, and there is usually loss of appetite, coating of the tongue, frontal headache, and sometimes nausea, though rarely actual vomiting. The conjunctivæ become injected and watery, and the eyelids probably red and swollen. Cough, often of a croupy character, hoarseness, and sneezing occur, together with a variable amount of nasal discharge. Diarrhœa is liable to arise at this stage, and is sometimes very

Temperature Curves in Two Cases of Simple Measles.



intractable, while epistaxis is not uncommon. Lachrymation and photophobia may be very pronounced, the latter a source of considerable discomfort, and the face not unfrequently presents a blotchy or "measly" appearance, best marked in the region around the mouth and nose. The aspect of a child during the early stage of measles is frequently very characteristic; he looks, as indeed he feels, the embodiment of human misery.

Now, the condition described above may persist throughout the pre-eruptive stage, but more often in benign attacks a distinct improvement sets in within forty-eight hours of invasion, characterised by a partial remission of temperature, and a lessening in the severity of the coryza and other catarrhal symptoms.

The improvement, however, is but temporary, for during the course of the third or fourth day, usually, in some cases a few hours earlier, the characteristic measles eruption begins to show itself, and its development is attended with an aggravation of both the febrile and catarrhal symptoms. The temperature rises rapidly as the eruption comes out, registering, perhaps, 104° F. or more within twelve hours. The cough, sneezing, and lachrymation become more pronounced; rhonchi may be heard over both lungs, and often moist râles in addition; the respiratory rhythm is accelerated. A sero-purulent discharge runs from the eyes, and the rhinorrhœa becomes thicker and more profuse. Diarrhœa is apt to recur, or it may now appear for the first time, and there is sometimes frequent desire to pass water, due, no doubt, to slight urethral irritation. There is always some enlargement of the lymphatic glands in the sub-maxillary, sub-mastoid, and cervical regions, but the swelling is rarely very great, or attended with much tenderness. These symptoms commonly reach their full development coincidently with the eruption, and the patient will in all probability be at his worst on the fifth or sixth day of the disease.

In most cases speedy improvement then sets in, the temperature being rarely sustained for much more than thirty-six hours after the first appearance of the rash. As a rule it falls rapidly, the normal being reached in favourable attacks at some time during the sixth day, or by the seventh morning at the latest. The drop of temperature is, however, often incomplete, but if delayed for more than a few hours, it usually indicates the supervention of pulmonary mischief.

The *eruption* presents the following characters:—It appears in the form of small red spots, usually first seen on the sides of the forehead and head at the margin of the hairy scalp, and on the

upper part of the neck behind the ears. The spots soon spread over the face, neck, trunk, and arms, for the most part in a downward direction, and lastly invade the legs and feet, the lower extremities being affected from twelve to twenty-four hours later than the face. As the rash develops, the individual spots become larger and distinctly papular. They coalesce with neighbouring ones in variable degree, and, as a result of their confluence, irregular raised tracts of red injected skin are presented, the intervening areas remaining pale and unaffected. The spots are often said to show a crescentic grouping, and this, no doubt, is as common an arrangement as any other which the imagination may suggest. The extent to which the face is involved varies a good deal; in some cases the spots are mainly confined to the forehead and chin. The circumoral region frequently presents a blotchy appearance, and is more often than not definitely invaded by the eruption. Both the flexor and extensor aspects of the limbs are affected promiscuously, and the rash is usually represented on the palms and the soles by a simple vivid flush. It may, however, in these situations, be of a spotted character, but is never distinctly raised.

The rash fades in the order in which it appeared, and rarely remains fully out for more than twenty-four hours at any particular spot. It will consequently have nearly disappeared on the face by the time it is reaching its full development on the legs. The actual eruption will usually have faded by the end of the week, but a brown or purplish mottled staining can usually be detected on the trunk and legs for several days, even a week or more, after the hyperæmia has disappeared. A fine scurfy peeling usually follows. This is rarely extensive, sometimes confined to the trunk; in other cases limited to the face and limbs, but it is never seen on the palms or soles. The peeling is usually completed within ten days after the rash has faded. It is sometimes stated that numerous small red points or spots with bluish-white centres may be detected on the palate or the inside of the cheek and lips for some hours, even three days (Koplik), before the eruption appears on the skin. They can be detected in some cases, but far more frequently they cannot, and usually nothing more can be made out than a catarrhal redness of the entire faucial and buccal mucous membrane, which has existed since the beginning of the illness.

In some attacks of measles the eruption is very transient and indistinct; indeed, it may be absent altogether.

Of the severe forms of measles two well-recognised varieties are

met with, viz. *pulmonary* and *toxic*. In the former, grave pulmonary implication is present from the outset; the breathing becomes extremely rapid, and the surface dusky. The temperature runs at a high level, and the pulse is very frequent. Fine crepitation can be detected all over the lungs without obvious dulness, dependent on widespread catarrh of the bronchioles, and general pulmonary congestion. The rash is often patchy, or it may be almost entirely suppressed. Cyanosis, drowsiness, and coma supervene, and death occurs before the week is out, in young children often preceded by convulsions.

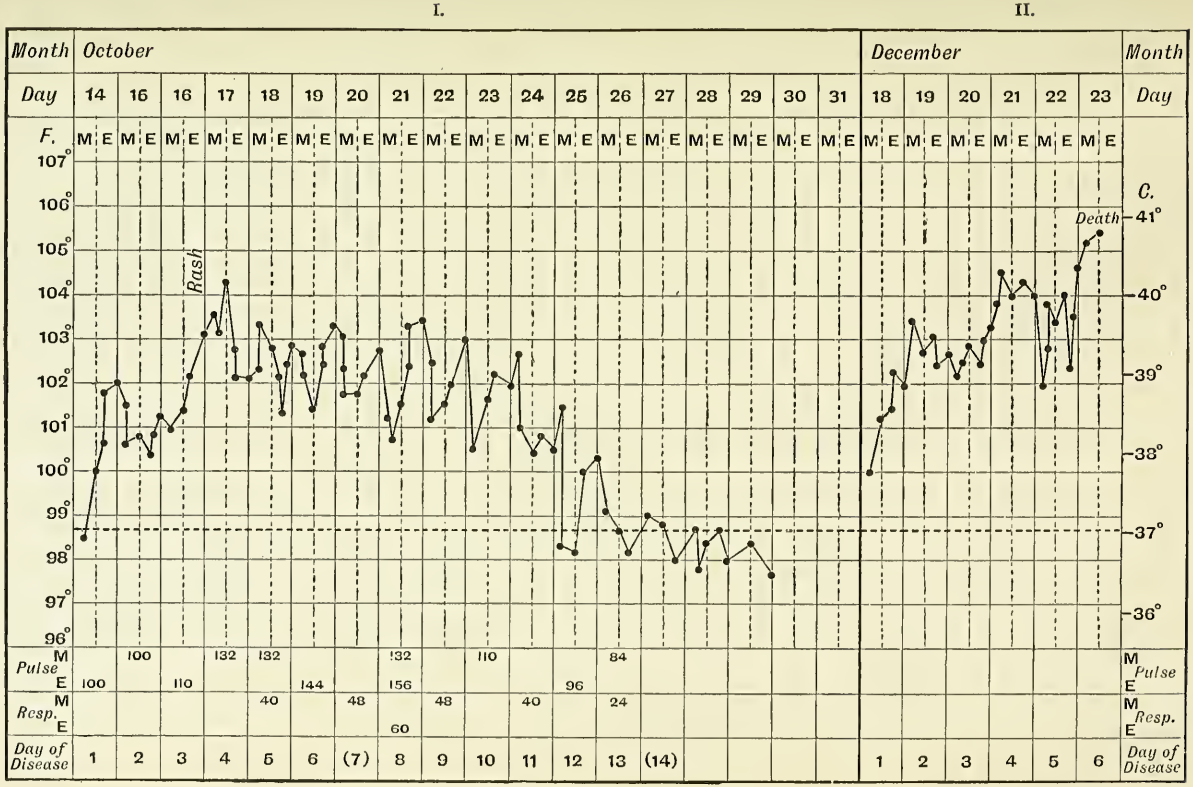
In the toxic form, a typhoid condition rapidly supervenes. The temperature is sometimes as high as 106° F.; the pulse becomes extremely feeble, often reaching 180 or 200, and the tongue dry and brown. The rash is intense, and soon becomes petechial; epistaxis is common, and muscular tremor pronounced. Delirium is present early, and soon passes into stupor, and the patient dies comatose on the fourth or fifth day. The variety known to the older writers as "black measles," if not hæmorrhagic smallpox, must undoubtedly have represented an extreme development of the toxic form of the disease.

Measles arising shortly after an attack of scarlet fever is often characterised by a higher mortality and a shortening of the pre-eruptive stage. The rash often appears on the first, and rarely later than the second, day of illness. When measles attacks a person who is just recovering from diphtheria, the condition is very serious, as there is great danger of the latter reappearing in the laryngeal form. Membrane rapidly spreads down into the smaller bronchi, and the case usually proves fatal; broncho-pneumonia in some degree being rarely, if ever, absent.

The **complications** of measles for the most part represent an exaggeration, in some cases an extension, of the catarrhal condition which is a normal feature of the attack. The most important are undoubtedly certain inflammatory affections of the respiratory organs, viz.—*acute laryngitis*, *capillary bronchitis*, and *broncho-pneumonia*, the symptoms of which in no way differ from those of the independent disorders. The laryngitis, however, may be membranous, in which case marked stridor develops. In some cases it is undoubtedly diphtheritic, while in others it is said to be due to the agency of pyogenetic micro-organisms.

Catarrhal stomatitis may develop, attended with the formation of shallow ulcers on the gums and adjacent side of the tongue or cheeks. In ill-nourished, or strumous children, though usually at a

Temperature Curves in Two Cases of Measles complicated by Broncho-pneumonia.



later date, severe gangrenous, or sloughing stomatitis, known as *cancum oris* or *noma*, may arise and lead to a fatal issue, perhaps attended with necrosis of the alveolar process, or even perforation of the tissues of the cheek; and the same condition may affect the vulva in female children. The nasal catarrh of measles may give rise to a chronic *muco-purulent rhinorrhœa*. Extension along the Eustachian tube frequently leads to *catarrh of the middle ear*, characterised by deafness, tinnitus, and otalgia. This often becomes purulent, hence *chronic otitis media*, perforation of the drum, and troublesome otorrhœa are common. The conjunctival catarrh sometimes leads to *phlyctenular conjunctivitis*, or it may develop into severe *muco-purulent ophthalmia*, attended with intense chemosis. *Keratitis*, or *ulceration of the cornea*, is liable to supervene, sometimes leading to hypopyon, and even, in rare instances, to panophthalmitis. *Diarrhœa* may become excessive, and even prove fatal through intensity of catarrhal enteritis. Certain affections of the nervous system are occasionally observed to follow measles in children, of which *chorea* and *muscular atrophy* of limited distribution, suggesting anterior poliomyelitis, are perhaps the most common; while both *diffuse myelitis* and *hemiplegia* of doubtful origin have been known to arise during the course of the attack. A peculiar form of *blindness*, unattended with any obvious lesion of the fundus or transparent media, has sometimes been observed in adults. *Phthisis*, *suppuration of the mastoid cells*, and *caries of the petrous bone* with its consequences, are all conditions for which an original attack of measles must often be held responsible.

Bacteriology.—The specific infecting agent in measles is doubtless a living microbe, but its identity has so far not been conclusively demonstrated. Canon and Pielicke in 1892 discovered a small bacillus in the blood and sputum of measles which they succeeded in cultivating. Their observations, however, lack confirmation, and it has been supposed by some that the bacillus was in reality that of influenza. Secondary invasion by septic and pyogenetic micro-organisms, however, is common, and to their presence most of the fatal complications of the disease must be ascribed. Moreover, both diphtheria and tubercle are liable to supervene during early or late convalescence, in each case showing characteristic lesions.

The **post-mortem appearances**, apart from its complications, are inconclusive in measles.

Prognosis.—The death-rate in different epidemics of measles is very variable. It varies from two or three to over fifty per cent

in proportion to the number of young children amongst those attacked, their social status and general physique, and the coldness of the season.

The influence of age is well shown by the following figures, quoted by Dr. Theodore Thomson, as representing the fatality of an epidemic affecting an urban population of 35,000 persons, amongst whom the compulsory notification of measles was in force.

Age in Years.	Percentage Incidence.	Percentage Fatality.
0-1	7.2	9.6
1-2	11.9	19.7
2-3	17.2 (13.7)	10.2 (8.5)
3-4	16.2	4.9
4-5	17 (2.8)	1.5 (6.1)
5-10	6.2	1.1
10 and over	.07	0.

Measles is most fatal during the latter half of the first, and the second years of life; after this the fatality rapidly declines until the fifth year is reached, when it almost ceases to exist. A rachitic, tuberculous, or syphilitic dyscrasia, or the presence of whooping-cough, diphtheria, or chronic lung disease, implies a high fatality.

Special symptoms which point to an unfavourable prognosis are, early high temperature without remission, early rapidity of breathing, cyanosis, rapid and feeble pulse, dry brown tongue, petechial eruption, severe diarrhœa, muscular tremor, stupor, and convulsions; while the supervention of any complication, such as membranous laryngitis, capillary bronchitis, broncho-pneumonia, or noma, is equally serious.

Diagnosis.—Measles, if unattended with a rash, may be difficult to distinguish from a simple cold in the head and chest, but such peculiarity of the attack is by no means common. The pyrexia of measles is usually more pronounced, and it may be possible to establish a connection with an undoubted attack. Only three of the eruptive fevers are likely to be mistaken for measles, viz.—rötheln, scarlet fever, and early smallpox.

From *rötheln* the distinction may be very difficult. Apart from any connection with a previous case, the following points are of value:—In rötheln, the degree of pyrexia and the severity of the catarrhal signs are less. There is an absence of pre-eruptive ill-

ness, the rash being usually the first sign, though tenderness of the cervical glands may have been complained of previously. The rötheln eruption is more transient, and presents features which are discussed more fully in the article devoted to the description of that disease (see p. 272).

In *scarlet fever*, vomiting is more likely to be present at the outset, and the rash appears within twenty-four hours of invasion. Coryza and respiratory catarrh are absent; the fauces are definitely inflamed, and perhaps actually ulcerated; while the glands under the jaw are usually enlarged and tender. The eruption is represented on the face by a simple vivid flush, the circumoral region remaining pale and unaffected. It never presents a spotted character on the palms or soles. The individual papules of the eruption are smaller and more closely aggregated, and though the papular element in parts may be well developed, the general surface of the skin presents a well-marked flush, which, as it fades, leaves behind a uniform staining rather than an appearance of mottling. The temperature shows a gradual decline as the eruption fades, instead of falling suddenly when the rash has reached its full development, as is the rule in measles. The peeling of the tongue is more complete, and the desquamation characteristic; moreover, the subsequent appearance of either adenitis, arthritis, albuminuria, or nephritis, are confirmatory of scarlatina.

Smallpox in its early stage is sometimes mistaken for measles, but the occurrence of a rigor, vomiting, and severe lumbar pain at the outset, the absence of catarrh, the appearance of the rash on the third day, attended with an immediate fall of temperature and a general improvement, are most distinctive. Moreover, in small pox the eruption can be felt in the skin before it is clearly visible, whereas in measles the spots are always macular before they become raised above the surface. Collie aptly compared the feel of the measles rash to that of velvet, in contrast to the sensation imparted by that of smallpox, which he likened to corduroy.

The **treatment** of measles is for the most part comprised in the endeavour to ward off its complications. The patient should be isolated as soon as possible, and placed in a room of fair capacity and easy of ventilation. He should be protected from draught, and the light should be subdued in view of the photophobia, which is often distressing. The temperature of the room should not be allowed to fall below 60° F., or rise above 70°; the atmosphere should be moistened with steam from a bronchitis kettle, and the patient lightly, but warmly, covered. If there be

much laryngeal irritation, a steam tent will prove most soothing, and a hot fomentation, or sponge wrung out of hot water, may be frequently applied over the larynx. In young children, if there be much bronchial affection, it is a good plan to encase the chest for the first few days in a light jacket-poultice, which should be changed every four hours. Many a young child's life has been saved by this means, and the benefit is often very striking.

In toxic attacks but little can be done beyond alleviating symptoms. Attempts to reduce the temperature by means of cold applications, though a source of comfort to the patient by reason of their sedative effect, have usually failed to cure. No drug has been proved to have any influence on the course of the disease. Restlessness, insomnia, and delirium, are indications for a nerve sedative, and either trional, chloralamide, or the wet pack may be used. Stimulants in small but frequent doses should be given in all really severe attacks, and whenever a patient is taking his nourishment badly. The treatment of the ordinary complications of measles calls for no special mention here.

F. Foord Caiger.

RÖTHELN

Syn Rubeola, Rubella, German Measles, Epidemic Roseola

Rötheln is a specific, infectious, and often febrile disorder, attended with a morbilliform eruption, enlargement of the lymphatic glands in the mastoid and posterior cervical regions, and occasionally slight catarrh of the ocular, nasal, and faucial mucosa.

It is almost invariably a mild affection, and seems to be unattended with any recognised complications or sequelæ. It occurs for the most part in temperate climates, and appears to be more common in Europe and North America than elsewhere. In our own country it is most prevalent in the spring and early summer, especially the months of April, May, and June. The disease in this country rarely shows the widespread epidemic prevalence which is so characteristic of measles, but commonly occurs in localised outbreaks, for the most part confined to the members of small communities, who are thrown into intimate association by reason

of various educational, trade, or administrative necessities. This probably depends upon the fact that the activity of the contagium is easily destroyed, and that close personal contact, under favourable conditions, is essential to effective extension.

Apparently no special susceptibility attaches to early youth; hence it is that outbreaks are no more common in schools than they are amongst the adult employés of Government departments, business houses, banks, workshops, clubs, and hotels, many of whom probably have never previously suffered from the disease. The presence of, or recent convalescence from, any acute disorder, such as scarlet fever, measles, or diphtheria, undoubtedly favours successful infection, whereas the fact of having once suffered from rötheln will almost surely protect from subsequent attack.

Much uncertainty has existed in the past as to the nature of rötheln. It has been variously held to be a modified form of measles, of scarlet fever—a hybrid of both—and a separate and specific infection. No other view but the latter is now tenable, and further discussion is uncalled for. It is unfortunate that greater unanimity has not prevailed in the past amongst those to whom we are indebted for its clinical description. It is evident that the descriptions given by Patterson in 1840, and the older German writers, apply, not to rötheln as we know it to-day, but apparently to a severe form of measles. Its features, however, are now pretty generally recognised.

The **incubation stage** may vary from seven or eight days to fourteen or fifteen, and, it is stated, even to twenty-two. In the writer's experience it has been most often ten days or a little over. In schools a quarantine of at least twenty days after removal of the last case is commonly insisted on.

Symptoms.—The attack usually commences with a feeling of malaise, and perhaps slight febrility, followed in a few hours by the appearance of the eruption. The rash, however, is often the first sign. The conjunctivæ are usually injected, and this may be the only evidence of catarrh; but more often the patient experiences the sensation of having a cold in the head, which at the same time may ache, and there may be slight cough, and more or less faucial discomfort. On examination of the throat, it is usually seen to be somewhat reddened and injected, and the tongue moderately coated. The glands beneath the jaw are rarely much enlarged, but those in the posterior cervical region, and the one lying over the mastoid bone, are both swollen and tender. In some attacks tenderness of the concatenate glands is complained of for several

days before the rash comes out, and, in rare instances, those in the axillæ and groins are also involved. The temperature at the outset may rise to 101°, or even a degree or two higher. It soon reaches its climax, and falls to normal again within forty-eight hours. In exceptional cases, particularly when there is much glandular affection, pyrexia of greater degree and persistence may be observed. Frequently, however, the temperature remains normal throughout the attack; and this occurs more often than is usually credited.

The *eruption* commonly appears first on the face in the form of small round or oval pinkish-red spots, and from thence spreads rapidly over the trunk and limbs, and finally invades the legs. The spots are but slightly raised, and soon coalesce; so that a uniform redness closely simulating the rash of scarlet fever is frequently to be seen on the lower part of the trunk, forearms, and legs. An occasional result of their coalescence is that irregular erythematous patches of variable extent and well-defined margin are presented. On the face the spots fade rapidly, as a rule, without previous coalescence; they are rarely very distinct for more than twenty-four hours, and the circumoral pallor may not have been encroached upon. In some instances the rash first appears on the trunk or limbs, in which case the face probably escapes altogether. The rash commonly fades within three, or at the most four days, leaving little or no staining behind, though definite peeling often follows. It is usually of a powdery or furfuraceous character, but "pinhole" peeling, indistinguishable from that of scarlet fever, sometimes, though very rarely, follows an undoubted attack of rötheln. The illness may be regarded as at an end when the rash has faded, and in many cases the patient cannot be said to have been ill at all. According to Forchheimer, a number of rose-red spots may often be seen coincidently with the appearance of the skin eruption on the mucous membrane of the uvula and soft palate. They are said to be about the size of a large pin's head, very little raised above the surface, devoid of crescentic grouping, and not to remain visible longer than twenty-four hours.

Pathology.—As to the nature of rötheln infection we know nothing, but infer that it is dependent upon the activity of some specific micro-organism. It is doubtful whether the disease is ever directly fatal; nor are any morbid changes in the blood, tissues, or internal organs recognised. The patient should be regarded as probably infectious for at least ten days after the appearance of the rash, and even longer, should any peeling remain. The occurrence

of a definite relapse has been occasionally recorded; but this, like a second attack, must be very uncommon.

The **diagnosis** of rötheln is often confused by reason of its likeness to mild attacks both of scarlet fever and measles.

It resembles mild *scarlet fever* in that slight faucial affection is often present; that the rash appears early in the attack, and is usually followed by distinct desquamation. The resemblance is most marked at that stage when the rash has faded from the face, and is present as a continuous flush on the trunk and limbs, with perhaps a distinct remnant of papulation. It differs from scarlet fever in that prodromal vomiting is rarely, if ever, present; faucial injection is less constant, and early cleaning of the tongue, much less a raw tongue, is wanting. The rash occurs on the face in the form of slightly raised spots, instead of being represented by a continuous vivid flush, which in scarlet fever neither presents a macular appearance, nor invades the oral circle. If seen at an early stage, the morbilliform character of the rötheln eruption will be apparent on the trunk. A complaint from the patient of tenderness, or pain in connection with the posterior cervical glands is most characteristic of rötheln; while the absence of "pin-hole" peeling, arthritis, nephritis, and adenitis during subsequent convalescence is confirmatory as far as it goes.

The resemblance between a case of rötheln and a mild attack of *measles* may be so close as to make a confident diagnosis in an isolated case impossible. This is especially true when the patient has recently had scarlet fever, as under these circumstances the pre-eruptive stage of measles is frequently curtailed, and consequently a valuable distinction is lost. The differences between measles and rötheln are of degree rather than of kind; hence the difficulty which may be encountered in their diagnosis. In rötheln, the interval between exposure to infection and the appearance of the rash is more often nearer ten days than fourteen, and the eruption appears on the first or second day of invasion, rather than the third or fourth. The individual spots of the eruption are usually smaller, pinker, more discrete (while still raised), less constant on the face, less persistent, and less staining, though liable to be followed by considerably more peeling.

The catarrhal symptoms, moreover, are less prominent, if not entirely absent; while distinct tenderness of the posterior cervical glands is the rule rather than the exception.

An attack of rötheln calls for no special **treatment**. The patient, if a child, should be kept indoors, and not allowed to mix

with others until at least a week or ten days has elapsed since the eruption faded. The desquamation may be hastened by the employment of warm baths and vigorous friction.

Although the vast majority of attacks are exceedingly mild, the possibility of rötheln taking a severe form must not be lost sight of. An outbreak, occurring in 1879, has been reported by Dr. Cheadle, the earlier cases of which were characterised by a severity surpassing that of ordinary measles. The attacks were mainly distinguished by severe affection of the broncho-laryngeal tract, giving rise to incessant croupy cough of a painful and harrassing nature, and by dusky red infiltrations of the faucial structures. Coryza, lachrymation, and intestinal irritation were practically absent, but excepting that the pre-eruptive stage was unduly short, the attacks bore in other respects more resemblance to severe measles. The writer met with similar cases in the year 1888, the diagnosis of which was most confusing. They occurred amongst a number of children convalescent from scarlet fever, and in some instances the attack proved fatal.

The term "epidemic," or "infective roseola," is applied by the Council of the Medical Officers of Schools Association to certain cases which they regard as entirely distinct from rötheln, though commonly confused with it. The cases occur in groups, usually in the summer time, and are characterised by absence of any prodromal symptoms, and of definite evidence of catarrh. The rash appears suddenly on the neck, limbs and trunk, the face usually escaping altogether. It consists of large rounded areas of bright red, closely aggregated spots, scarcely raised above the surface of the flushed skin. There is an absence of glandular swelling, little or no pyrexia, and the general health is hardly, if at all, interfered with. Whatever view may be taken as to the nature of these cases, they certainly sometimes occur in association with undoubted attacks of rötheln.

F. Foord Caiger.

SCARLET FEVER

Syn. Scarlatina

Scarlet fever is an infectious febrile disease, of which the most prominent features are inflammation of the faucial structures, a red punctiform rash, followed by characteristic desquamation, and a subsequent tendency to inflammatory affections of the middle ear, glands in the neck, joints, and kidneys.

Though showing a wide geographical distribution, the disease occurs but little in tropical regions. It is a good deal more prevalent in Europe, especially its north-western portion, and in America, than other parts of the world. Scarlet fever is rarely altogether absent from the larger towns of Western Europe, though periods characterised by its wider extension throughout the country at large tend to recur at irregular intervals; and in many of the large towns of Great Britain something approaching a local cycle is often apparent, the periods of greater incidence recurring every five or six years. In this country scarlet fever is most prevalent during the autumn and early winter months, the maximum occurring towards the end of October or beginning of November. It is least so during the spring and summer, the minimum usually being reached in either March or April. The fatality has shown a progressive diminution, at any rate in London, during the last fifteen years.

Etiology.—Infection is always derived from a previous case, either directly from the patient, or indirectly through some article of clothing or furniture, or perhaps a book or toy which has become contaminated with a minute particle of mucus, or of cuticle derived from his person. The degree of infectivity attaching to the faucial mucus, and particularly to any discharge from the nose or ear which has been present during the scarlatinal attack, is probably much greater than that of the desquamating cuticle, excepting, perhaps, that shed during the early period of convalescence. The epidermis, which separates during the later weeks, is apparently little, if at all, infectious, though the popular belief is to the contrary. Scarlet fever is sometimes conveyed by milk, many localised outbreaks having been definitely traced to a particular dairy. In no case has it been satisfactorily established that scarlet

fever has been propagated by means of defective drainage or an infected water supply. Infection is not very active before the rash is well out. The patient is probably most infectious at the height of the attack, and during the defervescence. Infectivity rapidly diminishes as convalescence proceeds, but the time at which a person actually ceases to be infectious is unknown. He should, however, be regarded as a probable source of danger so long as any discharge from a mucous surface remains, and as a possible source until his peeling is completed. The Medical Officers of Schools Association advise that isolation should be maintained for "not less than six weeks from the date of the appearance of the rash, provided convalescence is completed and desquamation has ceased, and there is no sore throat, discharge from ear, suppurating glands, or eczematous patches."

The following table comprises 81,605 consecutive cases of scarlet fever admitted into the hospitals of the Metropolitan Asylums Board during the six years ending 1897:—

Ages.	Males.			Females.			Total.		
	Admitted.	Died.	Mortality per cent.	Admitted.	Died.	Mortality per cent.	Admitted.	Died.	Mortality per cent.
Under 1 . .	443	110	24.8	362	98	27.1	805	208	25.8
1 to 2 . .	1,456	298	20.5	1,371	280	20.4	2,827	578	20.4
2 ,, 3 . .	2,631	406	15.4	2,553	383	15.0	5,184	789	15.2
3 ,, 4 . .	3,599	404	11.2	3,688	417	11.3	7,287	821	11.3
4 ,, 5 . .	3,862	314	8.1	4,140	281	6.8	8,002	595	7.4
Totals under 5 years	11,991	1,532	12.8	12,114	1,459	12.0	24,105	2,991	12.4
5 to 10 . .	15,791	495	3.1	17,592	523	3.0	33,383	1,018	3.0
10 ,, 15 . .	7,359	97	1.3	7,862	85	1.1	15,221	182	1.2
15 ,, 20 . .	2,366	36	1.5	2,368	35	1.5	4,734	71	1.5
20 ,, 25 . .	926	11	1.2	1,149	20	1.7	2,075	31	1.5
25 ,, 30 . .	420	5	1.2	657	7	1.1	1,077	12	1.1
30 ,, 35 . .	215	6	2.8	343	6	1.7	558	12	2.2
35 ,, 40 . .	91	2	2.2	140	3	2.1	231	5	2.2
40 ,, 45 . .	45	4	7.4	80	3	3.1	125	7	5.0
45 ,, 50 . .	26	2		23	1		49	3	
50 ,, 55 . .	17	1		17	...		34	1	
55 ,, 60 . .	5	...		4	...		9	...	
And upwards	1	...		3	...		4	...	
Grand Totals	39,253	2,191	5.6	42,352	2,142	5.1	81,605	4,333	5.3

The varying liability in respect to age is apparent. The largest number of attacks occurred in the second quinquennium of life, the first coming next, and then the third. After fifteen years of age the attacks were relatively few. All statistical records tend to show that the highest susceptibility to scarlet fever occurs during the fifth year of life.

The table further shows that females were attacked more often than males in the proportion of about fourteen to thirteen.

A definite second attack is occasionally met with, as is an undoubted relapse; but in most persons one attack of scarlet fever is sufficient to protect for life.

The **period of incubation** is usually three days, or a little less. It is said that it may be as short as twenty-four hours, and it is occasionally as long as six days. The Medical Officers of Schools Association recommends a quarantine of ten days subsequent to removal of the source of infection.

Clinical description.—From the clinical standpoint three varieties of scarlet fever are recognised, viz. the simple, the septic, and the toxic.

I. *Simple form*, or *scarlatina benigna.*—The *invasion* is commonly more or less sudden. The patient complains of headache, shivering, and aching pains in the back and limbs; the throat feels sore, and the act of swallowing is uncomfortable, if not actually painful; the tongue becomes coated and the appetite lost, and in most cases is attended with troublesome nausea, if not with actual vomiting. The association of headache, vomiting, and sore throat is most distinctive of the early stage of scarlet fever. On examination, the whole of the faucial mucous membrane is seen to be red and tumid, and the tonsils swollen—perhaps considerably. The temperature often registers 102° F. by the end of the first day, and the pulse is very rapid. The glands beneath the jaw are slightly enlarged, and probably somewhat tender. The rash usually appears within twenty-four hours of invasion, and is rarely delayed more than thirty-six. It comes out first on the chest, neck, and upper arms; and from thence spreads all over the surface in the course of the next twenty-four hours, for the most part in a downward direction. By this time the sides and tip of the tongue will have become red and raw-looking as the result of incipient denudation. Delirium of a quiet kind is not unfrequently met with in children, and is always associated with a high temperature. Together with the development of the eruption, both the faucial and glandular swelling and the general febrile signs increase, and the climax of

the attack is reached usually on the third or fourth night of illness.

A gradual improvement in all respects then sets in. The temperature slowly declines, the faucial tension abates, swallowing becomes less painful, the rash fades, and commencing desquamation becomes apparent. The duration of the febrile stage of simple scarlet fever, then, is about a week, though often a day or two less. The appetite is quickly regained as the throat improves, and convalescence proceeds rapidly.

In some undoubted attacks of scarlet fever there is practically no throat affection whatever, though the eruption may be extremely well developed; the temperature is but little raised, and the whole attack may be over within three days. This is characteristic of the cases often spoken of as "Surgical Scarlet Fever," which, though very mild, are certainly infectious.

The scarlatinal *rash* is of a bright brick-red colour, and consists of two distinct elements, viz. an erythematous flush and a number of minute, closely-set, injected papules, which, to a large extent, though by no means necessarily, correspond with the points of emergence of the hairs. The rash, consequently, has a distinctly punctate appearance. This will be more apparent in proportion as the erythematous element is wanting, and as the latter fades before the papular injection subsides, the punctiform character of the rash is usually best marked during the later stage. The eruption appears first on the chest, neck, and upper arms, and, spreading downwards, reaches the legs some hours later. It attains its full development in about two days,—that is, about the third evening of the disease,—from which time, or a day later, it begins to decline, and, fading in the order in which it came, is usually gone by the end of the week.

After the rash has disappeared a uniform greenish-yellow staining of the skin is left, best marked on the abdomen. This is in no sense a mottling. Where the skin is normally harsh, as on the outer side of the legs and upper arms, a number of coarse injected papules commonly remain for several days after the general eruption has faded. Occasionally some of the papules on the trunk and arms become distinctly vesicular, especially if the rash be intense and the patient have been sweating.

On the palms and soles nothing but a vivid flush is seen, punctation being exceedingly rare. Nor does punctation occur on the face; there the rash is represented by a red flush, which, though present to a slight extent on the forehead, nose, and chin,

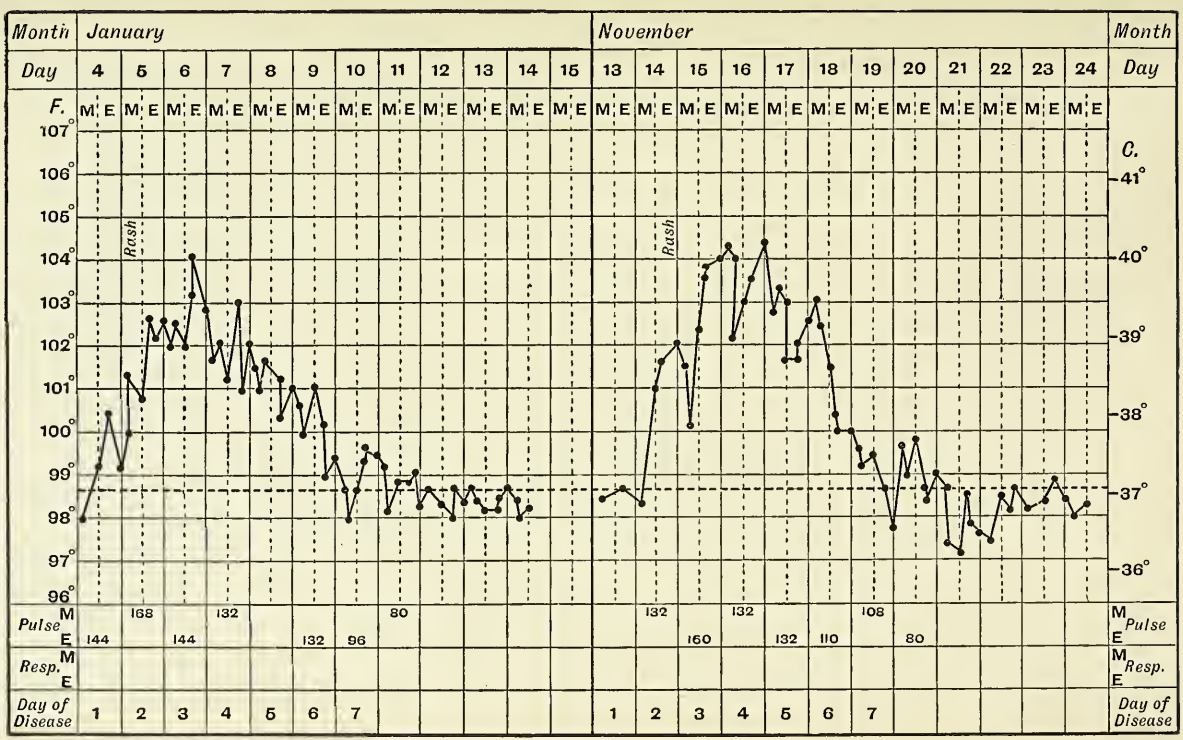
is most intense on the cheeks. It never invades the region around the mouth, which always remains pale and uninjected. This "circumoral pallor," which is strictly limited by the naso-labial folds, stands out in striking contrast to the vividly injected cheeks. It is an appearance seen in other febrile conditions besides the early stage of scarlet fever, notably in pneumonia; but at a later stage, viz. the second or third day of the rash, a fine powdering becomes apparent on the flushed surface, imparting a curious "powder and rouge" appearance to the complexion which is most distinctive of scarlet fever. In children of delicate complexion it closely resembles the bloom on a ripe peach, and is most becoming. The powdering is in reality the expression of incipient desquamation.

More or less *peeling of the skin* probably always occurs in cases which have been attended with a definite rash, its amount being generally proportionate to the intensity and persistence of the latter. In infants in whom the skin is velvety and contains a good deal of fat, peeling is usually slight and transient, and in adults is sometimes so insignificant as to be practically limited to the hands and feet. This is especially true of persons whose skin is naturally greasy, as in the subjects of acne punctata.

The character of the desquamation varies in different parts of the body. On the face, ears, and inner side of the upper arms, at any rate at an early stage, it is represented by a simple powdering of the surface. On the neck, trunk, and limbs it takes the form of delicate flakes or scales of variable size, preceded by a pin-hole or worm-eaten appearance of the cuticle which is very distinctive. Each "pin-hole" is caused by the mechanical rupture of the delicate epidermal covering of one of the papules comprising the eruption. From each of these centres peeling extends centrifugally, until, by fusion of their peripheries, any such ring-like arrangement becomes unrecognisable. From the palms and soles, where it is normally thick, the cuticle is shed in large patches or shreds, which may be continuous with that covering the fingers or toes, and so lead to the separation of an incomplete glove or golosh. On the palms and soles before actual separation occurs the surface becomes yellowish, dry, and wrinkled, suggesting in its appearance and feel a piece of old parchment. In some cases a dry chalky condition of the palms and soles is all that can be found to represent desquamation.

Desquamation is rarely completed until six or eight weeks from the date of the eruption, and occasionally not until the expiration of three or four months. The earliest sign of peeling, viz. the

Temperature Curve in Two Cases of Simple Scarlet Fever.



powdering on the face, can usually be detected by the second or third day of the rash. By the end of the first week peeling will be well marked on the face, neck, and upper part of chest. By the end of the second it will have become general. By the end of the fourth it is often complete, with the exception of the palms and soles, which, especially the latter, often require two or three weeks longer.

The *temperature* in simple scarlet fever rises rather rapidly, and usually reaches a climax on the third or fourth night. Defervescence then occurs gradually by lysis, and the normal is reached in most cases on the sixth or seventh day. The temperature shows a daily range of from one to two degrees, and the highest record is rarely above 105°.

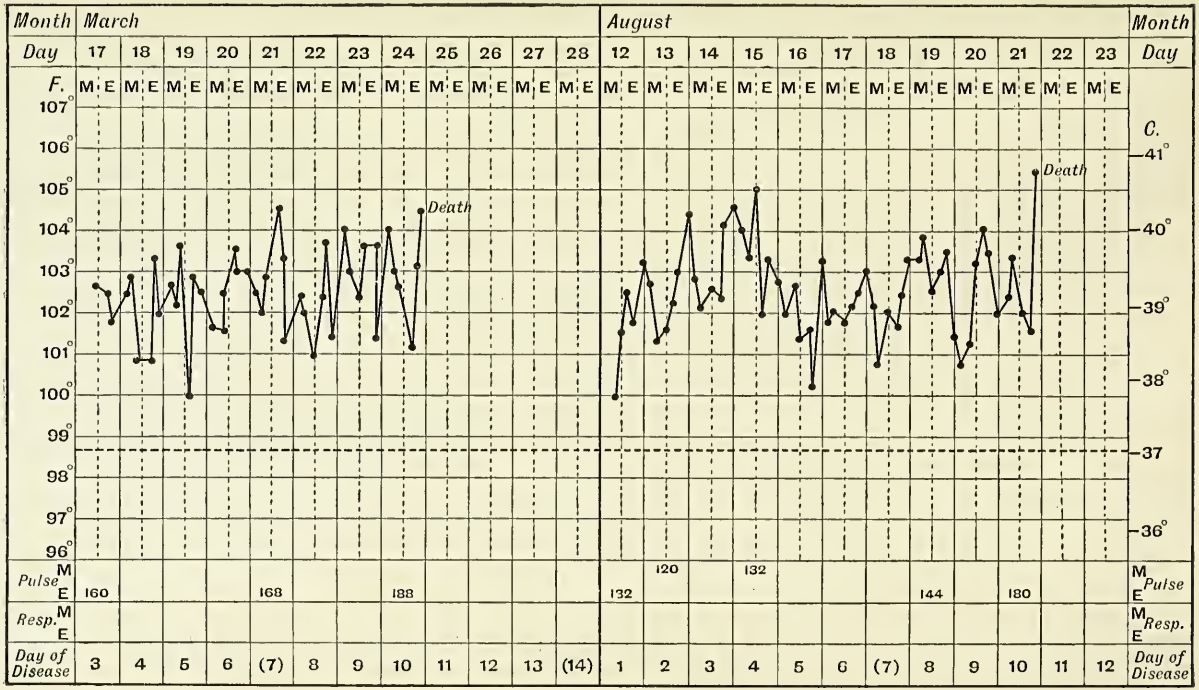
The scarlatinal *pulse* is characterised by undue rapidity in proportion to the degree of pyrexia. This, however, is only observed during the early stage of the attack. A pulse-rate of 144 to 160 in a child during the first two days of scarlet fever is in itself no cause for alarm.

In some attacks there is hardly any actual *swelling of the tonsils*, although they are usually somewhat red and tumid. In other cases the swelling is considerable, and if the inflammation be very acute their surface may become coated with granular fibrinous deposit, which is often mistaken for a diphtheritic exudation. Tonsillitis must, therefore, be regarded as a contingent, rather than a necessary factor in simple scarlet fever, though an essential feature in the septic form of the disease.

The appearance of the *tongue* in scarlet fever is most distinctive. It rapidly becomes coated with a thick white fur, through which some of the fungiform papillæ may usually be seen protruding. Denudation of the surface then begins, starting from the tip and edges, which are usually clean by the end of the second day, and, proceeding centripetally, the whole surface of the tongue becomes stripped of fur by the third or fourth day of attack. The tongue thus comes to present the raw denuded appearance which has been aptly compared to that of a ripe strawberry. Early in the course of the second week a renewal of its normal epithelium takes place, and the tongue resumes its usual aspect. The completeness with which the tongue peels is proportionate to the intensity of the previous inflammatory injection of the mucous lining of the mouth and fauces, just in the same way as the amount of peeling of the skin is regulated by the intensity and persistence of the antecedent eruption.

TEMPERATURE CURVE IN TWO FATAL CASES OF SEPTIC SCARLET FEVER.

I. II.



II. *Septic form*, or *scarlatina ulcerosa*.—In this variety the ordinary symptoms of scarlet fever are aggravated by the presence of faucial ulceration, which, in addition to being a serious lesion in itself, provides a focus from which septic material is absorbed into the system. The temperature, instead of declining during the latter half of the week, remains elevated and takes on an irregularly remittent character. The rash may be intense, and is often patchy, and delirium, combined with restlessness, is usually present.

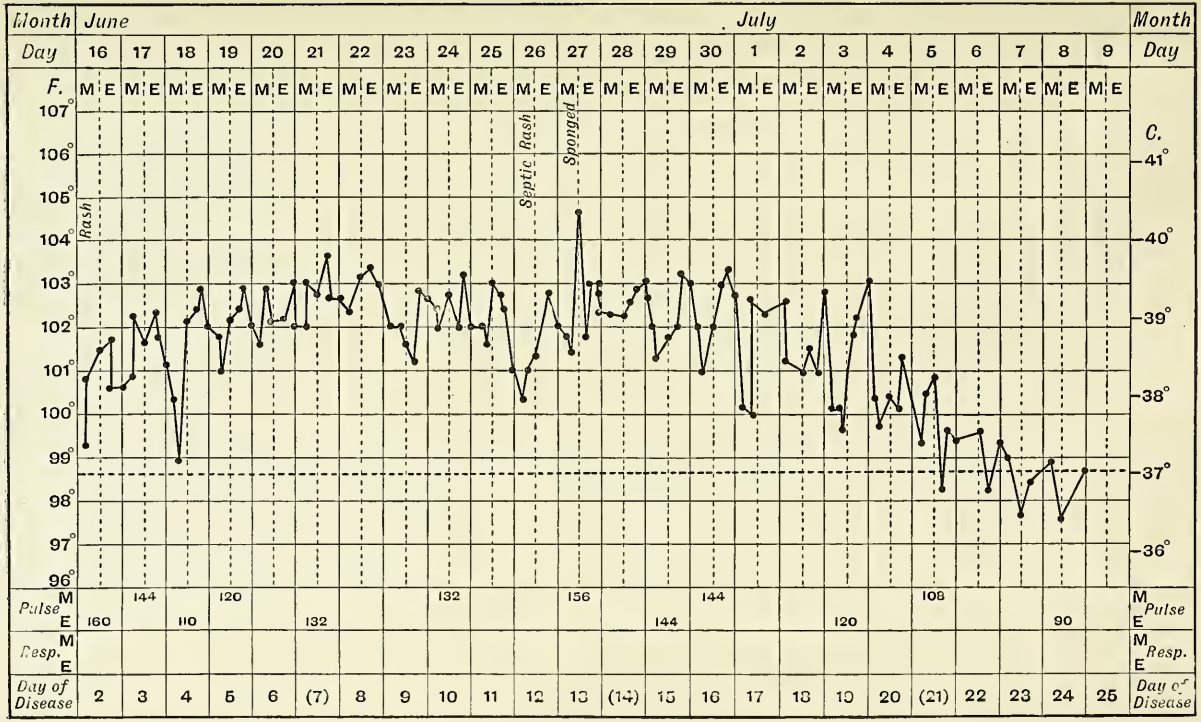
The most characteristic signs, however, are swelling, ulceration, or even necrosis of the tonsils, inflammatory infiltration of the subjacent glands and connective tissue, and a profuse muco-purulent or thin straw-coloured rhinorrhœa, the irritant quality of which often leads to excoriation of the external nares.

The tongue peels as in the simple form of attack, but a few days later becomes re-coated with a dirty white fur, which assists in imparting an offensive odour to the breath, while patches of superficial ulceration may develop on the sides of the tongue or at the angles of the mouth. At this stage there is often albuminuria, and diarrhœa is not uncommon.

Should recovery ensue, a gradual improvement in all respects sets in towards the end of the second week, or a few days later, attended with subsidence of the faucial and lymphatic engorgement, delirium, and pyrexia. The ulceration of the tonsils heals, and the patient is again able to swallow without distress and obtain the benefit of sleep. The severity of the tax he has undergone is revealed by the degree of weakness, loss of flesh, and anæmia which is present at the commencement of convalescence. This in some cases may not take place until the expiration of more than three weeks from the date of invasion.

In the worst cases the tonsillar ulceration takes on a sloughing character, attended with enormous infiltration of the tissues of the neck; so much, indeed, that the space between the upper border of the clavicle and the lower jaw becomes occupied by a collar of brawny induration. Or, again, the ulceration may spread, and thus involve the pillars of fauces, uvula, and soft palate, which, in some cases, becomes perforated, or, extending downwards, may cause extensive destruction of the tissues forming the upper opening of the larynx. The mechanism of the parts becomes interfered with in consequence, and any attempt at swallowing results in the passage of food into the nares, or through the laryngeal aperture. Nor is the patient able to sleep, because the moment he drops off he is suddenly

TEMPERATURE CURVE IN A PROLONGED CASE OF SEPTIC SCARLET FEVER.



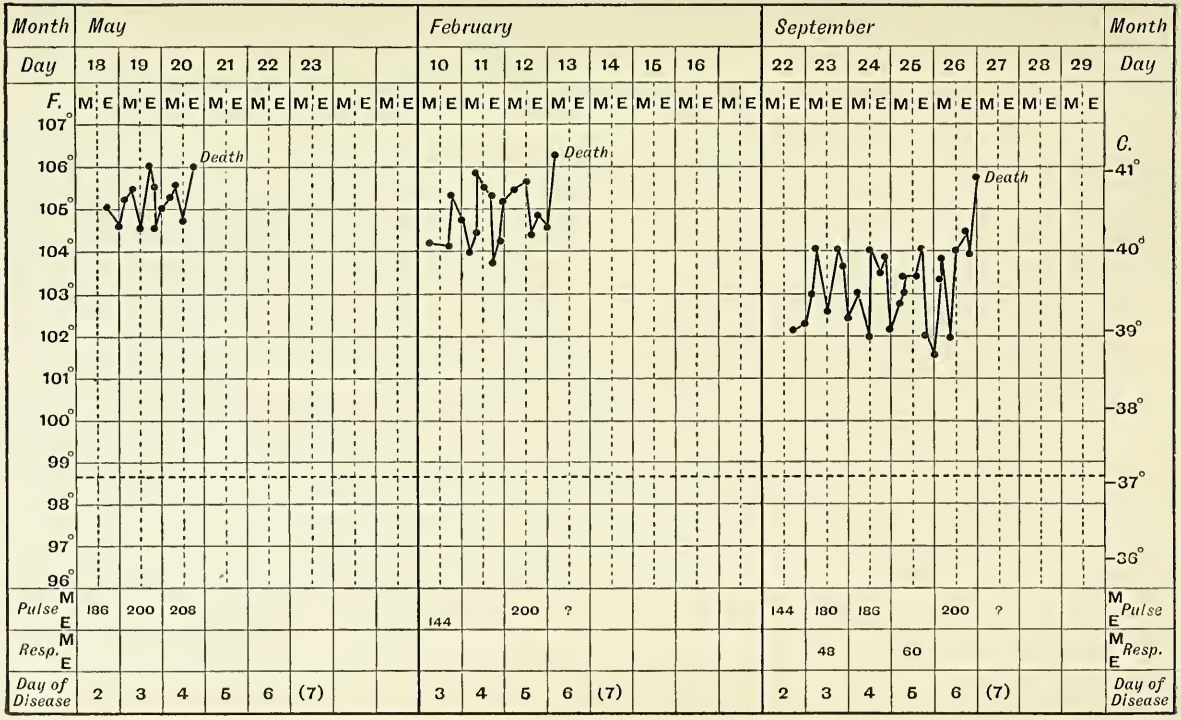
awakened, half choked, by the passage of irritant secretions into the larynx, or by the dropping back of the base of the tongue and epiglottis, with consequent obstruction to the breathing, since the nasal passages are blocked up with swelling and secretion. For its relief tracheotomy may be required. The exhaustion entailed by this constant distress, coupled with the severity of the disease, soon becomes extreme, and the patient rapidly sinks, death often occurring between the tenth and fourteenth days.

In cases which linger on, the septicæmic character of the attack becomes more pronounced; profuse sweats, diarrhœa, and great emaciation, albuminuria, pulmonary congestion, or septic broncho-pneumonia commonly arise before death, which may not take place until the end of the third week. Occasionally a pyæmic condition supervenes, characterised by the appearance of secondary abscesses in the glands, connective tissue, joints, or pleuræ. Moreover, a septic rash may develop during the latter half of the second week. It is sometimes erythematous, and more often morbilliform in character, and limited to the cheeks, buttocks, and extensor surface of the joints. About five out of every six cases attended with a septic rash are fatal.

III. *Toxic form*, or *scarlatina maligna*.—In this variety the gravity of the condition is out of all proportion to the throat affection, being dependent on the toxic intensity of the strictly scarlatinal poison. Cases deserving of the term "malignant," in which the patient is struck down and dies, perhaps, within forty-eight hours, before the typical symptoms of the disease have had time to develop, are extremely rare in this country at the present day; but we occasionally meet with attacks to which the term "semi-malignant" may be fairly applied. They are characterised by great severity, and usually prove fatal on the fourth, fifth, or sixth day of the disease.

The symptoms of invasion are unduly severe, especially the vomiting, which may be incessant, and usually persists to the end. The rash is very intense, with a tendency to become petechial as the case proceeds. The temperature is very high, and shows but very slight remission; it is often above 105°, rarely falling below 104°, and before death may rise to over 106°. The pulse is extremely rapid, in children often registering 180 on the first day of attack. The fauces are red, and vividly injected; but there may be very little swelling of the tonsils, while ulceration or marked infiltration of the subjacent lymphatic glands is exceptional. The patient is extremely restless. Delirium or stupor are always present, coupled

TEMPERATURE CURVES IN THREE CASES OF TOXIC SCARLET FEVER.



with pronounced muscular tremor. In adults the delirium is apt to be violent, and there is always great prostration. In most cases coma supervenes, and the case soon proves fatal. Cadaveric lividity sets in rapidly, often before life is extinct; it and the petechial character of the eruption are expressive of the intense toxic disintegration which has taken place in the blood.

Of the **complications** likely to arise in connection with scarlet fever, the following list enumerates their percentage incidence, among 30,417 consecutive attacks:—

Otitis media	14.74	Abscess	2.58
Simple albuminuria	8.26	Tonsillitis (secondary)	2.36
Cervical adenitis	5.66	Ulcerative stomatitis	2.12
Arthritis	3.75	Broncho-pneumonia	1.33
Acute nephritis	3.12	Bronchitis	1.21

With the exception of certain other infectious diseases to which the scarlatinal convalescent is very liable, viz. diphtheria, chicken-pox, measles, and whooping-cough, no other affection showed an incidence as high as 1 per cent.

Otitis media, like ulcerative stomatitis and broncho-pneumonia, is essentially a disease of young children, rarely arising after ten years of age. It is more frequent after severe attacks than mild ones, and, though the invasion may be acute, in many cases otorrhœa is the first and, indeed, the only symptom. The otorrhœa, if continued, may lead to suppuration of the mastoid cells; and ultimately, if neglected, be followed by thrombosis of the lateral sinus, pyæmia, abscess of the brain, or meningitis

Albuminuria, like acute nephritis, which is the expression of the same, though more severe, lesion of the kidney, is as common after a mild attack of undoubted scarlet fever as after a severe one. They most often arise during the latter half of the second and the third week, but occasionally somewhat later. Cold, in itself, seems to have but little influence; but in raw, damp, or even "muggy" weather the liability is greater. Acute nephritis associated with scarlet fever is noteworthy, in that hæmaturia is constant, and a relatively prominent symptom, whereas dropsy of any degree is rare, and complete recovery the rule under early and appropriate treatment.

The *cervical adenitis* referred to arises during convalescence, usually during the third and fourth weeks of illness, and is attended with a fresh rise of temperature. It is often associated with nephritis, and suppuration is not uncommon.

Arthritis, like secondary tonsillitis, usually affects adults and older children, especially females. Its time of onset is remarkably constant, viz. the fifth, sixth, or seventh day of attack, just when the temperature is falling to normal. The arm is more often affected than the leg, the smaller joints than the large, and the wrists and metacarpal joints most of all; the heart and pericardium are very rarely affected, and recovery is usually rapid.

An *abscess* may occur in any situation, especially after a septic attack. Its most frequent seat is in the glands of the neck and over the mastoid bone, in the latter case usually preceded by otorrhœa. Suppurative arthritis and empyema occur sometimes.

Ulcerative stomatitis is usually a mild affection; but in delicate children, though fortunately rarely, it may assume a sloughing character, and lead to alveolar necrosis or perforation of the cheek. Noma vulvæ is occasionally seen.

Broncho-pneumonia is prone to arise in the course of a septic attack in a young child, and is frequently fatal.

Chorea has been sometimes observed to follow scarlet fever. It is, however, an extremely rare sequela, and it is very doubtful whether the association can be regarded as more than accidental.

Bacteriology.—Scarlet fever is, no doubt, due to the specific activity of some micro-organism which multiplies within the system. So far, however, its identity has not been conclusively established, though Klein has demonstrated the presence in the blood and fauces, in certain cases of scarlet fever, of a streptococcus which he regards as distinctive. Its presence has been confirmed by other observers, but it is usually regarded as dependent upon the septic element which is present in most severe attacks.

There is reason to believe that the scarlatinal virus undergoes multiplication in the blood rather than in the throat or skin, though infection is doubtless transmissible through these channels.

The **post-mortem appearances** observed in the organs are not very distinctive of scarlatina, but are for the most part common to the febrile state. In the intestines, however, a distinct enlargement of the lymphatic follicles is noticeable,—perhaps more often than not,—and in rare instances ulceration. The kidneys present no constant appearance in scarlatina; but should any evidence of renal involvement have been apparent during life, signs of glomerular nephritis, with or without marked interstitial change, will be present, according as the case was fatal at an early or late stage of the disease.

The **general mortality** of an outbreak of scarlet fever, like

that of diphtheria, is mainly regulated by the comparative number of young children amongst those attacked, and the degree of poverty in which they exist. The fatality of scarlet fever at the present time in London at large is about 4 per cent. The case mortality of 81,605 cases treated in the hospitals of the Metropolitan Asylums Board during the years 1892-97 was 5.3 per cent (see table on p. 275).

The **prognosis** in an individual attack is influenced by certain personal factors, viz. age, sex, and state of health, apart from any inference to be drawn from the type of attack.

The case mortality progressively falls with each year of life until the time of puberty, from whence until about the thirtieth year it is at its lowest. Afterwards a slight rise occurs. In the series referred to above, the mortality for the first three quinquennia was 12.4, 3, and 1.2 per cent respectively.

The influence of sex is not very great, but the fatality amongst males is the higher.

Scarlet fever is very prone to take a bad form in ill-fed, strumous, and tuberculous subjects. Pulmonary tuberculosis, previously latent, is apt to be lighted up, and hurried to a fatal issue. During the puerperium there is a great tendency for scarlet fever to develop into fatal septicæmia. In persons suffering from chronic renal disease an attack of scarlet fever usually sets up fresh nephritis, which is very likely to prove fatal.

Severity of faucial swelling and ulceration, especially if attended with much adeno-cellular infiltration and a high temperature, is a bad sign, as indicating a septic attack; while extreme restlessness and persistent vomiting, with a petechial rash, high temperature, early mental impairment, and muscular tremor, point towards toxic intensity, and consequently danger to life. Delirium in an adult implies a severe attack, while convulsions in a young child, arising subsequent to the stage of invasion, are practically always fatal.

The differential diagnosis of scarlet fever from measles and rötheln is discussed in the articles relating to those diseases. Simple tonsillitis rarely affects young children, but in an adult may lead to confusion, especially if attended with a rash. The absence, however, of distinct punctation, vomiting, peeling of the tongue, and desquamation will usually decide its nature, while the appearance of arthritis towards the end of the week, or of albuminuria or nephritis during convalescence, point strongly to scarlet fever.

In the **treatment** of scarlet fever a specific virtue has been claimed for many drugs. None of them, however, have yet been

shown capable of exerting the least influence over the course of the disease. Happily, the large proportion of attacks are mild, and no active treatment is called for. It is usually sufficient to isolate the patient in a well-ventilated room, maintained at a temperature of from 56° to 60° F., to sponge the surface of the body over at least once a day with tepid water, and see that he is suitably fed and warmly, though not too heavily, covered.

Should the throat feel sore and the fauces be red and tumid, a mild astringent gargle or spray of boric, tannic, or weak sulphurous acid may be used every few hours. The constant sucking of pieces of ice, or the frequent sipping of an iced lemonade, containing a drachm of bitartarate and chlorate of potash to the pint, will prove distinctly comforting. A linseed-meal poultice or hot fomentation, renewed frequently, may be applied to the neck should tenderness of the glands be complained of, and the bowels should be regulated by means of a gentle aperient. The diet during the febrile stage should mainly consist of milk and beef-tea or broth, with the addition of jelly and grapes or oranges if desired; and a light solid diet containing fish, milk-pudding, bread and butter, and eggs may be allowed as soon as the temperature is normal and the patient is inclined to swallow it. From this time onwards a warm bath may be given every night with advantage. If the attack has been mild the patient may be allowed to get up at the end of ten days or a fortnight, and go out of doors a day or two later in fine weather. Care should be taken that he is warmly clad and does not get wet or sit about on a damp day.

In cases, however, in which the fauces are much inflamed, and especially if the tonsils are at all ulcerated, or even if they threaten to become so, energetic local treatment should be at once adopted with the object of preventing the development of a septic focus from which absorption would necessarily follow. To this end, nothing is better, or indeed so good, as the irrigation of the fauces and, if necessary, the nasal passages every two, three, or four hours with the acid solution of chlorate of potash, containing free chlorine, which is so useful in faucial diphtheria. It is made in the following proportions :—5 minims of strong hydrochloric acid poured on to 9 grains of powdered chlorate of potash, to which is gradually added, with frequent shaking, 1 ounce of water. Mixed with an equal volume of hot water, about half a pint of the solution is used on each occasion in the following manner :—

The patient sits up in bed with his head inclined forwards over a basin which he supports on his knees. Into his open mouth the

nurse, standing on the right side of the bed, with her left hand supporting his head, passes in a backward direction the nozzle of a four-ounce rubber enema bottle charged with the solution, which she then injects with moderate force so as to thoroughly wash out the faucial passage. The liquid runs out of the mouth and is caught in the basin underneath. Care should be taken to pause between each squeeze of the syringe, in order to allow the patient an opportunity of taking a breath. The irrigation is to be continued until the solution is used up; and, should there be any rhinorrhœa, the nasal passages must be treated in the same way, though more gently, and the patient directed to keep his mouth open in order to facilitate the return of the solution through the other nostril, rather than allow it to run down the throat and set up coughing through entering the larynx. By thus thoroughly flushing out the fauces, pharynx, and nasal fossæ at frequent intervals with an astringent antiseptic solution, all offensive secretions are cleared away, and the parts kept in a clean and wholesome condition; a result which cannot be attained by means of any gargle, spray, or swab. Should the chlorine cause vomiting, a half per cent solution of formalin with equal parts of water, or one of boric acid, may be employed; but neither are so efficacious.

The inflammatory infiltration of the glands and cellular tissue in the neck, which is frequently present in a septic attack, may necessitate incision. In such cases it is better not to wait for definite evidence of suppuration, but the brawny swelling should be incised in several places and tension thus relieved. Afterwards hot boric acid fomentations should be applied.

In young children it is sometimes necessary to feed by nasal tube or enema, in consequence of the difficulty in getting them to swallow, and in all septic attacks a little brandy should be given at frequent intervals.

In toxic attacks but little can be done beyond supporting the strength as far as possible by means of stimulants and concentrated nourishment. Unfortunately, the persistent vomiting so often precludes satisfactory oral feeding. The high temperature usually proves refractory alike to the influence of cold applications and of antipyretic drugs, but the cold pack is not without value as a sedative. The complications which are liable to supervene during convalescence from scarlet fever demand the same treatment as when arising independently.

F. Foord Caiger

ACUTE AND SUBACUTE RHEUMATISM

Syn. Rheumatic Fever

To understand the disease known as "acute rheumatism" it must be studied, first and chiefly, in the child. For in childhood it is more frequent, more varied, and more virulent than in the adult. The earliest period of life is, indeed, almost exempt, for rheumatic symptoms are hardly ever seen before two years of age. But if the frequency of rheumatism were represented by a curve, the vertical height of which indicated the number of cases at each successive year of life, it would be found that the maximum height of the curve would be at or about ten years. The rise to this height would be rather rapid, the fall much more gradual. At the age of forty the curve would nearly have reached the base-line. The manifestations of the disease are more varied in the child than in the adult; some of the phenomena fairly common in the former are rarely seen in the latter. It is also more virulent; an acute attack rarely proves fatal in an adult, but this is much less uncommon in children.

Clinical characters.—The invasion is moderately abrupt, sometimes preceded or accompanied by slight sore-throat. In a day or two the temperature rises to about 102°, vague pains are complained of, and the child loses appetite. There may be slight effusion, with pain and tenderness, in one joint, perhaps even in two or three, but the arthritic phenomena are often very slight, and may easily be overlooked altogether.

Yet even in the slightest cases *the heart* may be affected. An *acute dilatation* seems to be almost invariable. If the "deep" cardiac dulness be carefully delimited by light percussion, it will almost always be found to be larger than normal. In the healthy child this dull area extends from one finger-breadth (or rather less) to the right of the right border of the sternum in the fourth intercostal space to just within, or in children under seven quite up to, the left nipple-line. In the child suffering from rheumatism the heart will be found, on careful examination, to extend to the left of the nipple-line from a half to one finger-breadth, but the right limit is usually, in a first attack, unaltered. This indicates a definite dilatation of the left ventricle. The first sound at the apex is

altered in quality; it is less loud and clear than normal and usually shorter, though it may be prolonged into a systolic murmur. At the base the pulmonary second sound is too loud. The cardiac impulse is diminished in strength, and felt over too large an area; the maximum is in the nipple-line, or even slightly to the left of it. These phenomena may easily escape notice, but they are of great importance. They show that the affection of the heart in rheumatism is in no sense a "complication"; it is a characteristic, and the most important, part of the disease.

Greater severity of rheumatic attack in a child manifests itself less by increase of arthritis than by a fiercer assault upon the heart. Several (or even many) joints may be affected, but in children the arthritis is usually less severe and more transient than in the adult. The heart often sustains grievous damage, the effects of which are permanent. The acute dilatation is more marked than in the slighter cases, and is probably due to definite myocarditis, in addition to the toxic action on the cardiac muscle which seems to be the cause of the minor degrees of acute dilatation. *Endocarditis* is common, the mitral being almost invariably the valve first affected, causing a systolic apex murmur which tends to be conducted towards the axilla. This must not be confounded with the systolic murmur over the right ventricle, which is not uncommon in healthy children. A systolic murmur at the apex in a rheumatic attack may perhaps sometimes be due to anæmia, but endocarditis should always be suspected. After a time it may be observed in many cases that the systolic murmur is followed by a double second sound heard only at the apex. The first element of this double second sound is probably the normal second sound of the heart; the second element is probably produced by tension of a slightly thickened and stiffened mitral flap, resulting from the active ventricular dilatation which normally occurs at the commencement of diastole. The first element of this double second sound never changes its character as long as it is audible at all. But in many cases the second element becomes altered from the sharp sound of tension into a short blowing murmur, the effect of vibration of the stiffened mitral caused by the commencing inrush of blood from the auricle into the ventricle. Sometimes, and especially on auscultation a little more internally, this murmur in the early part of the diastolic period is found to be replaced by a similar short blowing murmur of presystolic time. This is no doubt produced by vibration of the stiffened mitral caused by the greater force of the blood current during the auricular systole, but it must not be taken to mean any definite narrowing of

the mitral orifice. After a while the doubling of the second sound at the apex disappears. This perhaps means that slight shortening has occurred in the valve or its chordæ, the result of contraction of the new fibrous tissue, so that its tension occurs earlier and again coincides with the normal second sound, or that the early diastolic murmur, growing more definite, commences at the earliest instant of the diastolic expansion and obliterates the second sound.

Pericarditis may occur even in a first attack. It is a symptom of danger, for it is usually associated with great increase of the cardiac dilatation, indicating probably a profound affection of the heart-muscle. The first evidence of pericarditis may be vomiting, or subjective distress, or a disturbance of the cardiac rhythm (so that it becomes triple or confused); or else an audible rub, heard over some part of the cardiac area, usually first at the base and later over the right ventricle, sometimes even at the apex and to the right of the sternum. The quality of the friction-sound is usually rough, often so rough as to resemble scratching or tearing, but at the base it may at first be so soft as to simulate a double aortic murmur. The cardiac dulness is almost always enlarged before the rub is heard, and it soon becomes further increased. It is possible that this increase may to some extent be caused by effusion of fluid into the pericardial sac, but post-mortem evidence shows that, though the whole heart may be covered with plastic lymph, there is rarely any great increase in the pericardial fluid, and that sometimes none at all is found even where the increase in the dulness is most extensive. On the other hand, marked dilatation is found to be very common, and extreme dilatation is not rare.[1] The outline of the precordial dulness affords very little assistance in determining whether fluid pericardial effusion is present in addition to the cardiac dilatation, but decided extension of dulness to the left of the sternum in the second and third intercostal spaces is in favour of some effusion, for this usually is most abundant at first about the great vessels.

Cases of rheumatism in which pericarditis and great dilatation of the heart are present often exhibit symptoms of grave *cardiac failure*, due no doubt to the damaged state of the cardiac muscle. Dyspnœa is marked, and may be extreme, even in the absence of any lung complication. It is probably the exaggeration of a normal reflex from the right ventricle to the respiratory centre, by which an overstrained right ventricle is automatically relieved.[2] The failure of the left ventricle is shown by the feebleness and frequency of the

[1] Vide *Med.-Chi. Trans.* 1898, p. 447. [2] *Lancet*, 1893, vol. ii. p. 1050.

pulse. Vomiting and delirium may also occur, the former probably of reflex origin, the latter analogous to the delirium sometimes seen at the end of a case of chronic heart disease. Fortunately, pericarditis does not often produce much pain, though it causes local tenderness. Coexisting pleurisy may cause pain. It is revealed by a pleural rub in one or both axillæ, or along the left border of the heart; in the latter position the rub, though of pleural origin, may be of cardiac rhythm. Rheumatic pleurisy rarely leads to much effusion of fluid, being in this respect similar to rheumatic pericarditis. Pneumonia is a somewhat rare complication; it adds greatly to the danger. Both the pleurisy and the pneumonia of rheumatism prefer the left side.

These affections of the thoracic organs are the points on which the attention of the physician ought to be primarily fixed when called to see a child suffering from even the mildest attack of rheumatism. The more external manifestations of the disease in skin, joints, and fibrous tissues, are not of vital importance. But they are often of much use in diagnosis, and some description of them is necessary to complete the clinical picture.

The affected *joints* are usually only slightly swollen. They are distinctly tender and painful, but neither swelling, tenderness, nor pain is equal to what is often observed in the same disease at a later period of life. There may be hyperæmic patches of skin over these joints, but they usually soon disappear. There may also be some pain and tenderness in the adjacent tendons, especially behind the knees. Pain and tenderness in the cervical spinal articulations or in the tendinous insertions of the cervical muscles may cause stiffness and immobility of the neck, simulating caries of the cervical spine.

In the neighbourhood of the joints, and in fibrous tissues elsewhere, children often manifest a form of rheumatic affection which is rarely seen in adults. Small, firm, slightly movable subcutaneous *nodules*, not painful, but sometimes slightly tender, are found over prominent bony points, especially over the ends of the long bones, the vertebral spinous processes, and the iliac crests; also in tendinous structures, such as the pericranium, the sternal aponeuroses, and the flexor and extensor tendons of the fingers and toes. They exist in about one-fourth of the cases of rheumatism in children. Sometimes only a single nodule may be discoverable, in other instances only two or three, but there are often many, and more than fifty may be present at the same time. The smaller nodules are of the size of a pin's head; the largest commonly met

with are about equal to a pea, though still larger ones are occasionally seen. There may be a simultaneous outburst of many nodules, followed by their gradual disappearance, and a subsequent appearance of a fresh crop. Some may vanish in a few days, others remain for many months or even for more than a year. The existence of many or of large nodules is certainly one of the indications of an intense rheumatic process, and makes it probable that serious progressive morbid change is occurring in the heart.

These nodules were carefully described, and their histological structure investigated, by Prof. Hirschsprung of Copenhagen in 1879, also by Dr. Barlow and Dr. Warner in 1881. They were found to consist mainly of fibrous tissue with some cells (round or spindle-shaped), dilated vessels, and a certain amount of nearly homogeneous, more or less fibrillated "ground-substance." Recently Dr. Poynton and Dr. Still have brought forward evidence to show that this homogeneous substance is in reality a fibrinous exudation, and therefore probably the manifestation of a local rheumatic inflammation. They thus confirm the suggestion of Drs. Barlow and Warner that these nodules are homologous with the inflammatory exudation which forms the base of a "vegetation" on a cardiac valve, and also with that found on the pericardium in rheumatic pericarditis. Occasionally quite unmistakable nodules have been seen both on the pericardium and on the mitral valve.

Rheumatic manifestations in the skin are not uncommon. Excess of sweating is sometimes observed, but is seldom profuse in children. A definite rheumatic eruption shows itself in not a few cases. It is usually an erythema ;—papular spots, or small circular areas with slightly raised hyperæmic margins and paler centres, or larger areas with irregular outline formed by coalescence ; it is perhaps most frequent about the joints, though it may occur on the trunk. In rare cases the erythema becomes vesicular or purpuric, or there may be numerous petechiæ, especially on the legs and feet. But erythema nodosum is probably not a manifestation of rheumatism, though it may occasionally be found in a rheumatic subject ; it appears to be an independent exanthem, with a pyrexial course of definite length and a characteristic eruption.

In the *muscles* vague pains may be felt, and some distinct atrophy is occasionally observed after a rheumatic attack. When there is also slight numbness and some defect of cutaneous sensibility, there is reason to suspect a local neuritis.

Tonsillitis, sometimes of the "follicular" variety, may precede or

accompany rheumatic symptoms, or there may be a generalised pharyngitis.

Anæmia is often a prominent feature of a rheumatic attack; it may be rapidly produced or intensified.

Chorea is frequently associated with rheumatism in childhood. The relationship between the two affections needs further elucidation, but the more carefully they are studied, the more intimate it is found to be. Choreic symptoms of slight intensity are common in children suffering from acute or subacute rheumatism, and when there is no definite chorea there may sometimes be seen the tendency to emotional disturbance, the causeless and transient fits of crying, which are so often observed in chorea. The onset of a severe chorea frequently follows two or three weeks after the occurrence of symptoms which, though slight, were definitely rheumatic. During an attack of chorea undoubted symptoms of rheumatism may manifest themselves. Many cases of chorea which have apparently, at the time, no connection with rheumatism, suffer from an attack of that disease a year or two later. After making allowance for possible coincidences, the conclusion is irresistible that there is some very close connection between the two diseases, and that in many cases chorea must be looked upon as a definitely rheumatic symptom.

A rheumatic attack which has been inadequately treated, or in which the treatment has been suspended too soon, is very apt to *relapse*. Symptoms which had almost or altogether subsided may return, or fresh rheumatic symptoms may show themselves. This is a fact of the greatest importance and one to be constantly remembered in the treatment of even the mildest cases. In some patients this tendency to relapse is specially strong, and can be overcome only by regular and persistent treatment carried on for a long time. Even after health has apparently been restored and all rheumatic symptoms have entirely subsided, there is in children a very strong tendency to recurrence of the disease a few months later, or after a year or two. Many have three, four, or more attacks. If rheumatism were simply an arthritis, this would perhaps be of little consequence. But the fact that in almost every attack the heart is more or less affected makes such recurrences a serious calamity. Too often the dilatation of the heart produced by the first attack has not subsided when a second attack dilates it further, even if no definite endocarditis or pericarditis is produced. Enormous dilatation may thus be brought about; the heart may extend nearly to the right nipple line and beyond the left anterior

axillary line, the left border rising two or even three finger-breadths above the left nipple. These dimensions can easily be demonstrated by careful percussion, and they are confirmed by autopsy.

In a *second or subsequent attack* of rheumatism, in addition to increased cardiac dilatation, there is often distinct evidence of permanent damage to the mitral valve, and reason to suspect fresh endocarditis. The systolic murmur is louder and conducted to the angle of the scapula; it is often accompanied by a much shorter blowing murmur of early-diastolic or of presystolic time. In some cases an aortic regurgitant murmur becomes audible, but this is much less common. At a later period the early-diastolic apex murmur tends to disappear, and the presystolic murmur becomes slightly vibratile, the vibrations becoming coarser as the years go by. But it is very rare to find in children under ten a churning murmur at all like that which is characteristic of the mitral stenosis of young adults. The narrowing of the orifice is a slow process and requires several years for its development.

Pericarditis is less frequent than dilatation and endocarditis, but it is the mark of a specially acute rheumatic attack, and it greatly increases the danger. It is usually accompanied by marked increase of the dilatation, and symptoms of cardiac failure are not far off. It rarely leads to any great amount of fluid effusion into the pericardium, in spite of the current teaching on this subject, which is founded on the erroneous assumption that the increase of the precordial dulness is entirely caused by effusion of fluid into the pericardial sac, and that it is an accurate indication of the amount of such effusion. Plastic lymph, more or less organised, is found in a fatal case, and often much thickening of the pericardium, but seldom much fluid, and sometimes hardly any at all. More or less pericarditis, old or recent, is found in about three-fourths of the fatal cases; in about one-half the pericardial surfaces are found to be entirely adherent.

Extensive venous thrombosis has been met with shortly before death in a few cases; Dr. Poynton has recently drawn attention to this.

Below the age of ten years, girls and boys are equally liable to suffer from rheumatism. But from ten to fifteen years of age, girls are twice as liable as boys to rheumatism, and three times as liable to chorea. This may possibly be in some way connected with the more rapid development of girls than of boys during these years, the girls gaining both in height and weight more rapidly than the boys. The greater liability of girls between ten and fifteen to

rheumatism and to chorea goes a long way to explain why mitral stenosis is so much more frequent in women than in men.

In adolescents, from fifteen to eighteen years of age, rheumatism is less common, for many of the most susceptible subjects have been already eliminated. It is also on the whole less virulent. Pericarditis is now less commonly fatal, but it often produces permanent crippling of the heart. Dilatation is almost invariable. Endocarditis is common. The evidence of former heart disease is often marked; it takes two forms. One is that of a dilated heart, with or without evidence of pericardial adhesions, with a loud, long systolic murmur at the apex. The other is that of a definite mitral stenosis, the presystolic murmur beginning now to assume its typical character. The two types may be combined. Nodules are less common than at an earlier age; arthritis somewhat more common.

In adults, arthritis is usually the most prominent symptom, and often causes much suffering. Many joints may be affected, one or two leading the way, and others becoming involved in rapid succession. The distribution of the arthritis is fairly, but not accurately, symmetrical. The larger joints, especially the knees, are most affected, but the smaller joints have no immunity. The synovial sacs, where the structure of the joint allows it, become distended with fluid; this is most marked in the knees, where it lifts the patella from the condyles and distends the suprapatellar sac, the normal outline of the joint being lost in a rounded swelling. The skin over the joint is generally pale, though it may be slightly hyperæmic. The tendon sheaths near the joint may also be affected. Movement of the affected joints is very painful. In slighter cases, the inflammation may leave the joint or joints first affected and appear in others.

Sweating may be general and profuse; it often causes a peculiar odour, especially when the patient is allowed to remain in an unchanged flannel night-dress. Sudamina and miliaria are frequently caused by the sweating. Erythema is occasionally seen; urticarial and purpuric forms of eruption are rare [1]; chorea is seldom met with in adults, nodules still more rarely.

The *urine* in acute rheumatism is scanty and of high specific gravity, soon becoming turbid with urates, and occasionally containing

[1] A case of very extensive bullous purpuric erythema, with pericarditis and fatal myocarditis, in a girl of seventeen under the care of the author, is reported (with an account of the autopsy and of the microscopical examination of the cardiac muscle) by Dr. Poynton in the *Lancet*, Oct. 28, 1899.

a trace of albumin. The tongue is often furred. Anæmia is rapidly produced by rheumatism, and is often a marked feature of the disease.

The predominance of the arthritis in adults has brought it about that acute rheumatism has been classed among diseases of the joints, and that the far more important cardiac affections have been considered as "complications." How essentially erroneous this view is a careful examination of the heart in almost any case of acute or subacute rheumatism will show. Even in a subacute case, in which there is very slight arthritis and hardly any pyrexia, determination of the so-called "deep" cardiac dulness by careful light percussion will almost always reveal an increase in size of the heart, which usually diminishes more or less when the attack is over, and sometimes returns to the normal. Accompanying this evidence of dilatation there is generally some alteration in the quality of the first sound, and the cardiac impulse is diffused and feeble.[1]

These facts prove that the arthritis of rheumatism is but one manifestation of a toxæmia, in which the central organ of the circulation is almost always more or less seriously affected. The physician must beware of being satisfied with the absence of murmur; the quality of the first sound must be observed, and a most careful examination of the heart, by percussion and palpation as well as by auscultation, must be made in every case. An acute dilatation, whether merely toxic or due to definite myocarditis, is a serious matter, and calls for prolonged rest and careful treatment.

Often the evidence of disease of the heart is obtrusive, even on the most superficial examination; but it is by no means easy to decide in all cases whether, or how far, the carditis is recent or of old standing. This is especially true with regard to dilatation and systolic murmurs. An increase of dilatation and a fresh endocarditis may very probably be part of the present attack. Fresh pericarditis is not very common in adults, and in them it is usually much less serious than in children, but an adherent pericardium is not uncommon. It cannot, however, be diagnosed unless there are also external adhesions fixing heart and pericardium to sternum, pleuræ, and lungs. It is probable that the greater part of the embarrassment of the heart usually assigned to adherent pericardium is due to myocarditis, old or recent, and increasing dilatation.

The results of chronic heart disease produced by previous attacks of rheumatism often add enormously to the danger of a later attack, and very greatly increase the difficulty of treatment. When chronic

[1] Vide *Med.-Chi. Trans.* 1898, pp. 401-417.

dilatation, mitral stenosis, or aortic regurgitation has existed for some years, compensation is apt to break down readily on the occurrence of even a slight fresh rheumatism, and congestion of the bases of the lungs, with indications of bronchitis or œdema, dilatation of the right heart, enlargement of the liver, sometimes dropsical effusion into the serous cavities or into the subcutaneous tissue of the lower limbs and of the loins, may manifest themselves.

The lungs and their serous covering suffer much less in rheumatism than the heart and pericardium. Pleuritic friction sometimes occurs, and is painful; but there is rarely much fluid effusion. Pneumonic consolidation of lung is met with in a few cases.

The *temperature* in rheumatism is variable. In a large proportion of cases it is comparatively low, not exceeding 102° F., often not over 100°, and it rapidly falls to normal under treatment. But even with this very moderate pyrexia acute cardiac dilatation is usually present, and severe pericarditis may exist. The temperature chart in this disease furnishes no trustworthy indication of the extent of the damage to the heart which is being produced. Yet there is one very important reason why it should be closely watched; in some cases the temperature rapidly rises, and it may run up in a few hours to 107°, 108°, 109°, or even 110° F. Death may quickly follow, unless some method of cooling the patient is used immediately. As hyperpyrexia comes on there is usually a tendency to delirium, and often a marked subsidence of the arthritis. A warning of the onset of this grave complication is frequently to be found in the cessation of perspiration, the skin becoming hot and dry in a patient who had been previously sweating profusely. Headache, sleeplessness, and restlessness should also be considered as warning symptoms. Rheumatic hyperpyrexia hardly ever occurs in a child, which is remarkable, for a terminal hyperpyrexia is by no means uncommon in some cerebral affections in infancy and early childhood. Occasionally, however, a case of chorea may end in hyperpyrexia, sometimes preceded by distinct rheumatic symptoms, sometimes alone.

Symptoms strongly suggestive of meningitis, such as strabismus, opisthotonos, muscular spasm, and final coma may occur in rheumatic hyperpyrexia, and even when the temperature does not exceed 104°, but actual inflammation of the cerebral membranes is very seldom found post-mortem.

The arthritis of acute or subacute rheumatism usually subsides completely when the attack comes to an end, which may occur spontaneously, as was shown in the cases "treated" with mint-

water in the presalicylic days. But this spontaneous recovery was often very slow, as indicated by the well-known story of the physician who was asked what was good for rheumatism, and replied "six weeks." Those who remember how rheumatism behaved before the introduction of salicylates will acknowledge that this was no great exaggeration. The shortening of the duration of a rheumatic attack by the use of the salicylates is marked and unquestionable.

But it must be added that the subsidence of a rheumatic arthritis, treated or untreated, is not always complete. Occasionally, in what seems to be a subacute rheumatism affecting several joints, one joint remains swollen and painful long after all the others have recovered, and it may show indications of structural changes. Some cases of this kind are not truly rheumatic, but are a gonorrhœal arthritis; others are the initial stage of the disease known as "chronic rheumatoid arthritis." Whenever "rheumatism" settles down into a chronic arthritis of a single joint, one or other of the above-named diseases should be suspected. The relationship of true rheumatism to "chronic rheumatism" affecting many joints and crippling them with fibroid thickenings of ligaments and tendons, and also to the chronic myalgias of later life, is a subject with regard to which further precise investigation is needed.

Until recently acute rheumatism was regarded as essentially an arthritis, and the painful, tender, swollen joints, the acid sweats, the furred tongue, the scanty urine loaded with urates, and the pyrexia, were thought to be the essentials of the disease. Pericarditis and endocarditis were looked upon as "complications." But when the malady was carefully studied in hospitals for children, it became evident that this view was far too narrow, that in early life arthritis is a comparatively insignificant part of the disease, and that the damage to the heart is more frequent and severe than in adults. More recently it has been shown that the rheumatic state manifests itself not only by arthritic and cardiac lesions, but also by various other clinical phenomena formerly regarded as complications, or as of merely accidental occurrence. In opening the discussion on "Rheumatism, and its Allies in Childhood," at the meeting of the British Medical Association in 1883, Dr. Barlow, in an exhaustive paper, showed that erythema (and occasionally urticaria and purpura), stiff neck, slight pains referred to the muscles, tonsillitis, subcutaneous nodules, and chorea are frequent and characteristic evidences of rheumatism in childhood. Dr. Cheadle summed up the results of his long experience at the Hospital for Sick Children

in lectures on "Heart Disease in Children," published in the *Lancet* in 1885, and again in his Harveian lectures (1888) "On the Various Manifestations of the Rheumatic State, as exemplified in Childhood and Early Life," in both of which he emphasised the importance of these non-articular evidences of rheumatism in childhood, and showed how the various members of the "rheumatic series" may occur in varying sequence and combination. He also insisted on the frequency and importance of an inherited predisposition to rheumatic disease, and pointed out that evidence of such inheritance, combined with the presence of some of the non-articular manifestations of rheumatism, is sufficient to prove the rheumatic origin of many cases of heart disease in which no history of arthritis can be obtained. The late Dr. Sturges, in his Lumleian lectures in 1894, laid great stress on the cardiac inflammation caused by rheumatism in children, and on the high mortality thence resulting. When it was observed that in rheumatism there is usually, if not invariably, an acute dilatation of the heart, even in subacute cases with trifling pyrexia and slight symptoms, it became evident that the most important part of this malady is its toxic action on the heart, and the resulting inflammatory condition of this organ.

Pathology.—The true nature and origin of this disease are still unknown; but the facts already stated make it certain that no neurotic theory and no theory of perverted metabolism can fully account for the phenomena: these strongly suggest a microbic infection. The greater frequency and greater virulence of rheumatism in childhood remind the physician of the infectious fevers, and the occasional occurrence of sore throat and of a characteristic eruption, with the pyrexia, are other points of resemblance. In its ill-defined course it resembles tuberculosis. In its tendency to produce acute dilatation of the heart it resembles influenza. The arthritis of rheumatism is very closely simulated by the arthritis produced by the gonococcus. No microbe has yet been proved to be the cause of rheumatism; but the same is true of such undoubtedly microbic diseases as measles, scarlet fever, whooping-cough, and syphilis. The strongly-marked hereditary predisposition to rheumatism causes no difficulty, for the same fact is observed in tuberculosis. That exposure to cold and wet is often a factor in the causation of a rheumatic attack is analogous to what is often observed in pneumonia.

Rheumatism has a certain relation to season, the maximum number of cases in London occurring in October and November.

It is also more prevalent in some years than in others. For an elaborate analysis of the available statistics on this subject reference may be made to Dr. Newsholme's "Milroy Lectures."[1] The times of greater prevalence are probably times when the conditions of temperature and moisture of the soil are specially favourable to the development of certain microbes.

It seems not unlikely that rheumatism may be a house disease, the germs being endemic in damp, ill-drained dwellings, extending upwards along damp walls, or being carried by air-currents from the soil. It would be interesting to inquire whether the disease ever occurs in houses with impermeable basement.

Recurrences of rheumatism may be fresh infections, or they may be caused by renewed activity of germs lying dormant in some part of the human organism, as occurs with regard to tubercle. As the pneumococcus may be found in the saliva of many persons who have suffered from pneumonia, so the rheumatic microbe may be lurking somewhere in the patient who has had rheumatic fever. As a man who has been infected with syphilis is always syphilitic, so a patient who has once suffered from rheumatism may be permanently rheumatic, and the temporary diminution of his power of resistance by a chill may suffice to produce a second attack.

It should be noted that rheumatism does not excite suppuration; the inflammatory effusions which it causes are all of the fibro-serous type. If suppuration occurs in a joint believed to be affected with rheumatic inflammation, either the diagnosis is erroneous or a mixed infection has taken place.

It has long been known that rheumatism produces a disastrous effect on the heart, and that endocarditis and pericarditis are frequent results; but far too little attention has been paid to the condition of the cardiac muscle, and a careful investigation of this, by the most recent histological methods, is greatly needed. In four recent fatal cases Dr. Poynton found (along with plastic pericarditis) very definite myocarditis; loss of striation with much fatty degeneration of the cardiac muscular fibres, and dilated capillaries with numerous foci of small cells in the interstitial tissue, not merely near the pericardium, but also *throughout the entire thickness of the cardiac wall.* These observations suggest that rheumatic myocarditis is not due simply to extension from an inflamed pericardium or endocardium, but is a primary lesion. If this be so, it is a fact of the greatest importance. It seems probable that the damage to the muscular substance of the heart is the true explanation of the

[1] *Lancet*, 1895.

destructive action of rheumatism. It is easy to understand how the injury to the cardiac muscular wall reveals itself clinically in an acute dilatation, a condition which often remains as a permanent chronic dilatation, and becomes the most important element in the cardiac failure of chronic heart disease. It is, however, by no means certain that an actual myocarditis is present in the cases which recover, and especially in those of slight intensity. The dilatation observed in subacute cases may possibly be due to a minor degree of toxic action on the muscle without myocarditis. In an investigation published in the third volume of the *Physiological Journal* (1880), Dr. Gaskell found that a dilute solution of lactic acid (1 in 10,000) produced marked dilatation in the frog's ventricle, and also in its arterioles, while a dilute solution of sodium hydrate caused contraction of both. He found that some drugs acted like lactic acid, others like sodium.

It has long been suspected, though on insufficient grounds, that lactic acid is the poisonous element in rheumatism, and Dr. Gaskell's observations indicate that it would produce the acute dilatation which actually occurs. But it seems more probable that the poison is a toxine produced by a microbe, and that the poisoning of the tissues in rheumatism is a selective action of this toxine, analogous to the selective action of the toxines of diphtheria and of tetanus.

Since endocarditis and dilatation are so characteristic of the rheumatic heart, great doubt must be felt as to the rheumatic origin of cases in which the pericardium is found to be entirely adherent and greatly thickened, with extensive mediastinal adhesions, but where the valves are normal, and the heart is small. One case of this kind recently examined post-mortem at the Hospital for Sick Children was found to be of tuberculous nature.

Prognosis.—A rheumatic attack in a child is much more serious than in an adult. In early life the mortality from cardiac rheumatism is very considerable. The prognosis as to life or death in such an attack must be mainly founded on a careful examination of the heart, especially with regard to its size and strength. The important points are: (1) The amount of cardiac dilatation; (2) the strength and localisation, or the feebleness and diffusion of the impulse; and (3) the presence or absence of pericarditis. Endocarditis has but little bearing on the immediate prognosis, unless it be of the malignant variety, which is rare at this age. Mitral stenosis and aortic regurgitation are seldom so advanced in a child that they can to any great extent influence the prognosis as to recovery.

The condition of the heart when acute rheumatism has subsided

is of great importance as the basis of an opinion as to the limitation of life or of capacity for active exertion which will result. But the most careful estimate is only too likely to be falsified by the occurrence of another attack of rheumatism, involving increased injury to the heart. It must, therefore, be constantly borne in mind that evidence of an active rheumatic toxæmia is of the greatest importance from the point of view of prognosis, and that such evidence is by no means limited to the question of arthritis, but that it may be manifested by sore throat, erythema, rheumatic nodules, chorea, pleurisy, pericarditis, endocarditis, and especially by acute dilatation of the heart.[1] After two or three such attacks, very great dilatation may be produced, and pericarditis, then supervening, may rapidly cause death.

In *adolescents* there is less likelihood of a fatal result from a rheumatic attack; but the presence of valvular disease (mitral regurgitation, mitral stenosis, less commonly aortic regurgitation) makes the prognosis more serious. Marked cardiac dilatation, and adhesion of the pericardium, both to the heart and to the sternum, pleuræ, and lungs, increase greatly its gravity. The least hopeful cases are those in which there is much dilatation, with a loud systolic apex murmur, and evidence of external pericardial adhesions: such patients rarely survive to adult life. The most hopeful are those in which dilatation is slight, external pericardial adhesions absent, and a mitral systolic the only murmur: such cases may have permanent compensation and live for many years, some even to old age. Mitral stenosis of high degree is of evil prognosis, especially if the right heart is more dilated than hypertrophied, and the liver has become enlarged. Mitral stenosis of low degree with efficient compensation may permit the patient to live to forty years, in a few instances even longer. The great majority of the cases of mitral stenosis in which no history of rheumatism or chorea can be obtained are almost certainly the result of a slight, perhaps relapsing, rheumatic endocarditis which escaped observation because pain and arthritis were absent or so slight as to have been entirely forgotten. Mitral stenosis is probably never of congenital origin; it would be safe to assert that no one has ever heard a presystolic murmur in a baby.

In *adults* a rheumatic attack is not often directly fatal, unless the heart is already much diseased, or hyperpyrexia supervene. The patient will almost certainly survive; but his future condition will

[1] It must not be inferred from this statement that rheumatism is the *only* cause of acute dilatation of the heart in a child.

depend to a great extent on the amount of the injury to the heart. The mechanical effects of damaged valves will assert themselves as time passes, but the chronic dilatation is in itself a factor of great importance. And in adults also, though less frequently than in children, the pernicious effect of a fresh rheumatism may sometimes be seen, entirely altering the prognosis previously formed.

Treatment.—Complete rest in bed is the first essential; this must be insisted on, even in the slightest cases, especially in children and adolescents, and the practitioner must not allow himself to be misled by the trivial nature of the arthritis. The condition of the heart must be at once ascertained, its exact size defined by careful light percussion, the position and character of the cardiac impulse noted, the quality of its sounds, and of any murmurs present observed. The temperature must be taken, and a chart at once instituted. For a rheumatic patient, a mattress is better than a feather bed, and cotton sheets are preferable to linen. The patient should be protected from draughts. Where there is much sweating, a flannel jacket should be worn over the night-dress, and the latter should be changed as required. In the severer cases the assistance of a trained nurse, strong enough to lift the patient, is necessary. The diet should at first consist of milk and beef-tea only. If constipation is present, a laxative may be administered; but active purgation should be avoided. If there is no constipation, a single 10-grain dose of pulvis ipecacuanhæ co. may be given (to adults) for the relief of pain, and it may sometimes be repeated with advantage.

Sodium salicylate should be given immediately, in doses proportioned to the age: to children, about three-fourths of a grain for each year, to adults in doses of 20 grains. This drug appears to be as definitely antagonistic to the rheumatic process as mercury to the syphilitic or quinine to the malarial. With the salicylate it is useful to give sodium bicarbonate, in a dose twice as large as that of the salicylate. The medicine should be taken hourly for the first three hours, afterwards every three hours, during the day-time; during the night also, if the patient is awake. When the temperature has fallen to 99° F., and the joint-pains have subsided, the frequency may be reduced to thrice daily, and this should be continued for a week or ten days after the pains have disappeared. Too early discontinuance of the salicylate is very often followed by a relapse of the symptoms —clear evidence of the power of the remedy. Necessity for reducing the dose of salicylate is indicated by deafness and tinnitus, sometimes by vomiting, occasionally by delirium, and in a few cases by irregu-

larity of pulse. If any of these symptoms are present, smaller doses of the salicylate should be given; but it should not be omitted altogether, if this can possibly be avoided. Care, however, should be taken to ensure that the drug used is of good quality, and free from adulteration.

It is thought by some physicians that salicylate is depressing to the heart; probably a large part of the cardiac depression supposed to be produced by the drug is really caused by the action of the rheumatic poison, leading to toxic dilatation and myocarditis, especially in hearts already damaged by previous rheumatism, and suffering from chronic dilatation or serious valvular disease. No doubt some patients are specially susceptible to the action of salicylate as others are to that of quinine or of morphine; but as a rule, in the earlier attacks of rheumatism the doses above mentioned may be given without fear of bad effects. If it seems necessary to omit the salicylate, salicin may be substituted; but it must be given in larger doses (30 to 40 grains for adults), or quinine may be given with alkalies in an effervescent mixture. Occasionally a small dose of calomel may be useful.

The joints should be wrapped in cotton wool and kept at rest. Only when an arthritis tends to become chronic should counter-irritation be used, by small blisters or a moderately strong iodine solution applied in the neighbourhood of the joint. Small doses of potassium iodide may be of service for chronic pains about the joints.

The heart must be carefully examined every day. If pericardial friction become audible, an ice-bag should at once be applied over the precordial region. The ice-bag must be water-tight, with an accurately-fitting screw top; it should rest directly on the skin, and should be surrounded with cotton wool or a soft towel to absorb the moisture which condenses on its outer surface. The area to which it is to be applied should be outlined on the skin, and the nurse must see that its position does not become shifted when the patient moves. If there is much tenderness, the ice-bag may be suspended so as to just touch the skin, but after a few hours it will be possible to apply it thoroughly. For young children hot-water bottles must previously be placed in the bed, so as to keep the feet and legs quite warm; the temperature should also be taken every half-hour at first. If pericarditis is present when the case comes under observation, and there is much cardiac dilatation, it will be wise to apply leeches before having recourse to the ice. The use of the salicylate is not to be omitted on account of pericarditis. In first attacks of rheu-

matism it is usually possible to keep the ice-bag continuously in position; but in later attacks, when there is much dilatation present, it must be removed at intervals. It may be applied for two or for three hours, removed for one hour or for two, then reapplied, in accordance with the condition of each case. Sometimes it is better to omit it altogether during the night; but it is desirable that the application of the bag should be as persistent as possible. In many cases it may be applied for a week or ten days, or even longer, with great benefit to the patient. It is probable that the local use of ice not merely controls the pericarditis, but that it also tends to check myocarditis, and it may sometimes be used with benefit for the latter purpose in a rheumatic attack in which there is acute dilatation but no pericarditis. Whether its influence extends as deeply as the endocardium is doubtful; but we have no other means of arresting endocarditis. If pericarditis is accompanied by pleurisy or pneumonia, an additional ice-bag should be placed over the inflamed lung or pleura, and the strain on the right side of the heart should be relieved by the application of leeches over the liver.

If ice cannot be obtained, small doses of opium or hypodermic morphine are advisable to quiet the distress, and leeches should be applied over the heart. It is uncertain whether blisters are of any real service in the treatment of pericarditis, and they greatly impede the examination of the heart.

Surgical measures are never necessary in rheumatic pericarditis, and they are extremely dangerous on account of the great cardiac dilatation. In suppurative pericarditis, on the other hand, they are urgently necessary, and may save life.

In the later attacks of rheumatism, when there is tumultuous action of the heart, great dilatation, and much cardiac distress, opium or morphine, in small doses, often gives great relief. This may be followed by digitalis; but it must be clearly recognised that the mere presence of a murmur is not to be taken as a signal for the employment of this drug.

If the temperature is persistently high and rising, especially if, at the same time, the arthritis subsides and the skin becomes dry, the temperature must be taken every half-hour. When it reaches 105° F., the patient should be sponged with cold water and covered only with a sheet; if this is insufficient to arrest the rise, decided measures must be taken at once. When a bath can be obtained, and the patient is not too heavy, it may be filled with water at 80° and the patient immersed in it for fifteen or twenty minutes, the water being meanwhile cooled to 60° by the addition of lumps of ice. During

this time his temperature should be frequently taken by a thermometer in the mouth; as soon as this reaches 102°, he should be taken out of the bath, replaced in bed, and covered with one blanket, with a hot bottle to his feet. The temperature will fall 2° or 3° further after his removal from the bath. The procedure must be repeated as often as necessary. It is sometimes more convenient to cover the bed with a large Mackintosh sheet, and to lay the patient absolutely naked upon it, sousing him all over with ice-cold water or rubbing him with lumps of ice. The temperature in the mouth must be frequently taken during this process.

Prolonged rest in bed is of the greatest importance after a rheumatic attack, especially if pericarditis, fresh endocarditis, or much acute dilatation has occurred. In such cases it is well to keep the patient in bed for an entire month after the temperature has become normal. The tendency to relapse is best averted by administering one or two daily doses of the salicylate for three or four weeks; in some cases it is needed for an even longer period. Provided this be done, it is safe and useful to prescribe iron for the anæmia, the best preparation being the dialysed solution of iron, given in drachm doses (to adults), in glycerine and water, after meals. If the heart has suffered damage, gentle "resistance-movements," repeated once or twice daily, should be practised for two or three weeks before any active exertion is allowed.

Children who have suffered from rheumatism, especially if any injury to the heart has been caused by it, need careful regulation of their life both at home and at school. The danger of a second attack, which will almost certainly cripple the heart still more, must always be kept in mind by the physician.

D. B. Lees.

CHICKEN-POX

Syn. Water-pock, Glass-pock, Varicella

Chicken-pox is an infectious, though usually mild, febrile disorder, attended with an eruption of papules, which, for the most part, rapidly develop into characteristic vesicles. These, after a few days, dry up and form scabs, which ultimately separate, and sometimes leave behind more or less persistent scarring of the skin.

Although the disease was described by Ingrassia as far back as the year 1550, it was not until the latter half of the eighteenth century that its specific distinctions from smallpox were clearly recognised; and even since, the two affections have often been confused. The prevalence of chicken-pox seems to be regulated by no known influences. Neither season nor climate appear to be operative. The association of susceptible persons with one suffering from the disease, and this under circumstances favourable to personal contact, are the only conditions which are known to be concerned in its diffusion.

Susceptibility to infection varies with the state of a person's general health, and whether or no he has had a previous attack. Chicken-pox is particularly liable to attack a child recently convalescent, or while actually suffering, from scarlet fever, measles, or diphtheria, if accidentally exposed to infection. The protection conferred by an attack is probably more complete than it is in the case of any other infectious fever, with the possible exception of whooping-cough. A second attack of chicken-pox is extremely rare, although an instance is recorded in which a person was three times attacked with the disease. Age does not appear to exert much influence, though the large proportion of attacks occur between the second and fifth years of life. The disease is rarely seen in adults, probably because most grown-up persons have already suffered from the disease in their childhood. Both sexes are attacked indiscriminately. The infection of chicken-pox does not seem to be readily conveyed indirectly. The disease, however, frequently arises in a sporadic fashion, it being quite impossible to trace any connection with a previous case. Its inoculability is doubtful.

The length of **incubation** in chicken-pox in the large pro-

portion of attacks varies between the limits of thirteen to fifteen days, but it may be as short as ten, or as long as nineteen. A quarantine of twenty days should be insisted on.

Symptoms.—An attack of chicken-pox may be either *mild* or *severe*, the severity of the attack being commonly proportionate to the amount of the eruption; in other words, to the number of the pocks.

In some attacks the eruption is the first symptom of the disease, but frequently the child may be noticed to be fretful and its temperature slightly raised for a few hours before the rash comes out. Occasionally, conjunctival injection or an erythematous flush on the trunk may be noted as well. This pre-eruptive stage is rarely of twenty-four hours' duration, but in adults the symptoms may be really severe, in which case pain in the back, shivering, headache, and weariness, attended, perhaps, with a temperature of 102°, or even more, may be present for two clear days before the eruption declares itself. In such instances the invasion closely simulates that of smallpox, and the rash as a rule is copious.

The chicken-pox *eruption* comes out in successive crops of slightly raised pinkish-red papules of variable size, most of which in a few hours become converted into characteristic thin-walled, limpid, glistening vesicles. Some of these develop so rapidly that the papular stage may escape observation, in which case the vesicles resemble little delicate blisters, such as might develop on the skin as the result of drops of scalding water. Others are obviously situated upon a red, injected, and slightly raised base, the central portion of which alone may have become vesicular. Some of the papules, especially the smaller ones, never develop into vesicles at all, but remain as small red, acuminate, or irregularly pyramidal pimples until they fade away. At the very earliest stage the papules appear as small, round, or ovoid spots, which, before becoming obviously raised, can be felt as slight points of thickening in the superficial layers of the skin. The individual pocks reach their full development at about the end of two days, after which the contents of the vesicles become turbid. They then rapidly shrink and dry up, forming brownish, horny-looking scabs, which usually separate at the end of a week or ten days. A slight areola can, as a rule, be seen around the base of the fully developed vesicle, which is sometimes, though usually not, umbilicated. If the vesicle be pricked, a thin clear fluid readily escapes, and the walls entirely collapse under pressure with the finger, though a slight thickening of the skin at its base is still

clearly distinguishable. The contents of some of the vesicles when fully developed may become purulent, in which case the areola is more pronounced, and a more or less permanent depressed cicatrix remains after the scab has become detached. Suppuration of the pock invariably results if it be scratched or otherwise ruptured, and this most often occurs on the face and scalp.

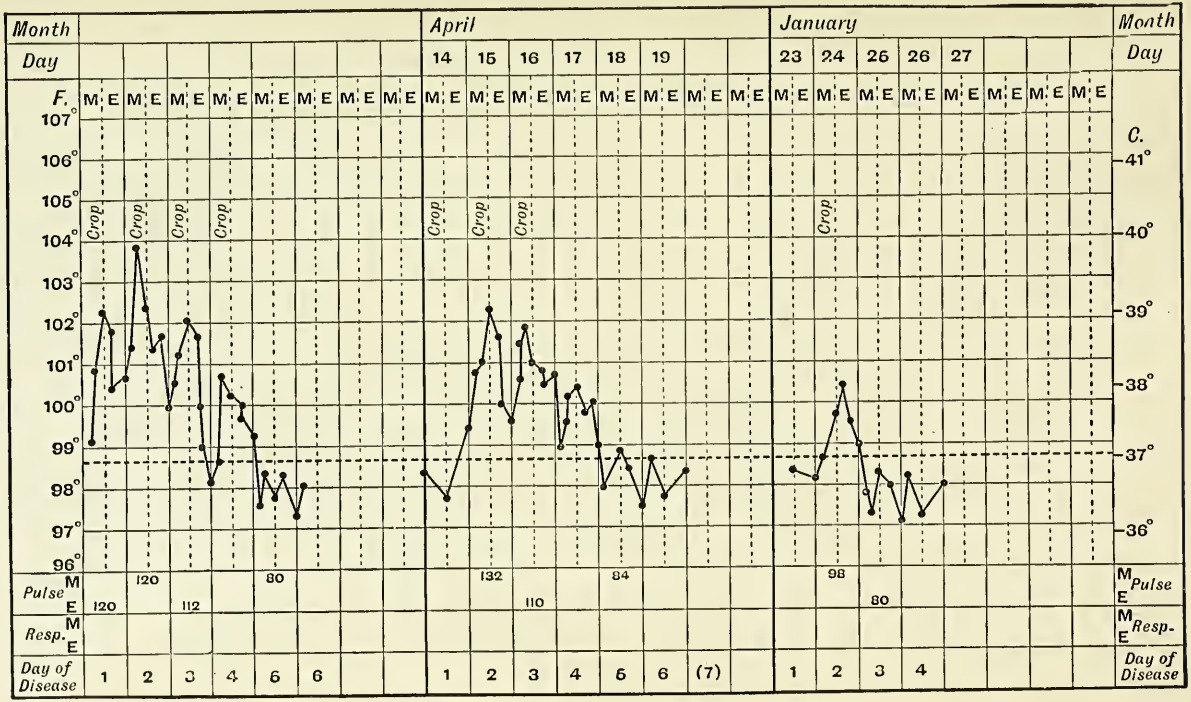
The eruption, perhaps oftener than not, comes out earlier on the trunk than elsewhere, but spots may appear first on the face and scalp, or even, though far more rarely, on the limbs. Ultimately the whole surface of the skin may be invaded, but it is usual for the eruption to be relatively more copious on the trunk, thighs, and upper arms than the face, scalp, or extremities. It is not common for the palms or soles to be affected, unless the rash be fairly extensive, and even then the spots may never get beyond the papular stage.

The mucous membranes may also be invaded, especially those of the palate, tongue, and buccal surface of the cheek. No true vesicle is found, however, but the pock is represented by a white sodden-looking papule, which usually breaks down into a shallow ulcer, and then rapidly heals. Pocks occur, moreover, though far more rarely, on the conjunctivæ and the mucous surface of the genitals. A peculiarity of the chicken-pox eruption is that it comes out in several crops, perhaps three or four, commonly on succeeding days; or an interval of a day or two may elapse between two consecutive crops. Hence it is that the length of the stage during which the eruption is coming out is commonly three to five days, though sometimes longer. The writer has seen it extend in one instance to ten days, and even longer periods have been recorded. The total number of pocks may vary from half a dozen or so up to several hundred. MacCombie states that the number is frequently from fifty to two hundred. The aggregate number of pocks will depend upon the number of crops, and may be taken as a measure of the duration and of the general severity of the attack.

The appearance of each crop of spots is commonly attended with a rise of temperature, perhaps to 100°, or 102°; sometimes higher. The temperature usually falls in the interval, if not to the normal, to something very near it. The second exacerbation is usually the highest, and a few pocks can then generally be seen on the mucous membranes, the subsequent ones, should there be any, becoming gradually less pronounced. The pyrexia of chicken-pox, then, is an irregular one, and if prolonged, shows wide daily variation. In some cases, especially when the rash is sparse and com-

Temperature Curves in Three Cases of Chicken-pox.

I. II. III.



prised in a single crop, the temperature remains normal throughout. Some acceleration of pulse accompanies the pyrexia, and the tongue is usually lightly furred. The eruption may lead to slight enlargement of the lymphatic glands adjacent to any of the pocks which have suppurated, and is often attended with considerable itching and consequent irritability of temper in young children.

In rare instances some of the vesicles are inordinately developed, and form distinct bullæ of varying size. They may even attain the size of a hen's egg, in which case a raw denuded surface of corresponding area remains after the fluid is let out. The condition closely resembles pemphigus, and is sometimes described as a variety of chicken-pox under the name of *varicella bullosa.* Attacks of chicken-pox are occasionally met with in which a necrotic change occurs in the skin forming the base of the pock. A certain number only are affected in most instances, but in some, almost all of them undergo the same change. The attack begins in the ordinary way, but as the case proceeds, the inflammatory areola surrounding an affected pock gets larger and more intense, and the vesicle is converted into a dark brownish, and ultimately, black scab, which gradually becomes thickened and enlarged so as to resemble a rupial crust. The underlying skin is found to have become gangrenous, and from its margin a thin sanious or blood-stained discharge escapes. After the slough has separated a clearly defined punched-out ulcer remains, which may extend superficially or in depth, and lead to a considerable loss of tissue. In fatal cases the temperature remains elevated, emaciation becomes pronounced, and the patient gradually sinks. The condition is known as *varicella gangrenosa*, and is usually fatal; but if a few pocks only are affected, recovery will probably ensue. Occasionally in these severe attacks an effusion of blood into the skin at the base of the pocks and from some of the mucous membranes has been recorded, a condition to which the term *varicella hæmorrhagica* has been applied.

The only **complication** worth recording is a condition of impetiginous eczema, which sometimes supervenes, probably as the result of dirt or scratching, although various affections have been observed to arise shortly after chicken-pox, such as nephritis, pneumonia, bronchitis, hemiplegia, and paraplegia; their connection with the disease is very much open to doubt.

Bacteriology.—No micro-organism has yet been satisfactorily established as the specific infecting agent. Both staphylococci and streptococci occur in the vesicles, as they do in those of smallpox

and vaccinia, and a bacillus which normally inhabits the epidermis. Protozoa and an oval coccus have been described, and Bareggi of Milan claims to have isolated the latter and by its injection to have successfully communicated the disease to children.

No morbid changes in the viscera special to varicella are known; nor does the disease ever seem to be fatal, except in the gangrenous or hæmorrhagic forms. In the former variety, which is probably determined rather by the constitutional predisposition of the particular patient than by any augmentation in the virulence of the specific contagion, the gravity is proportionate to the number of pocks affected.

The differential **diagnosis** of chicken-pox and modified smallpox is fully discussed in connection with the latter disease (p. 324), but the importance of the following points justifies their special mention.

In chicken-pox, pocks in all stages of development, macule, papule, vesicle, pustule, and scab, can often be seen side by side within a restricted area. In chicken-pox a tense, fully developed vesicle may be found at a spot on which twenty-four hours previously not even the suggestion of a papule could be detected. Second attacks of chicken-pox are so exceptional, that the diagnostic value of a few scars in a doubtful attack can hardly be overestimated. Concerning the nature of such scars, it is rare at the present day in this country to find a person bearing the marks of antecedent smallpox, especially if well vaccinated; moreover the cicatrices of variola are usually more abundant on the face than elsewhere, whereas in chicken-pox the reverse obtains.

A case of *varicella bullosa* may closely simulate pemphigus, but the presence of one or more normal pocks associated with the bullæ will decide its real nature.

The **treatment** of simple varicella is comprised in the prevention of the patient from scratching his pocks. In the gangrenous form the administration of stimulants and a generous diet will be necessary, and the affected pocks should be dressed with warm boracic fomentations. The patient should be isolated until all the scabs have separated. This usually means a detention of from two to three weeks.

F. Foord Caiger.

SMALLPOX

Syn. Variola

Smallpox is an acute, specific, contagious disorder, characterised by pyrexia and by the appearance, after a definite period of incubation, of an eruption which passes through the successive phases of papule, vesicle, and pustule.

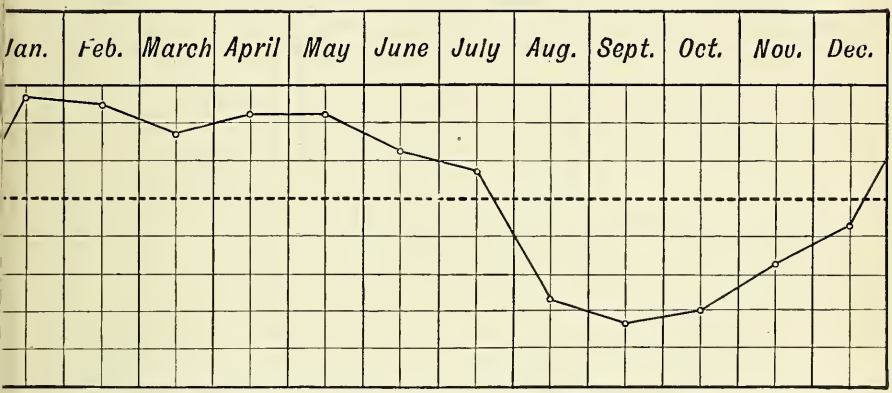
Smallpox affects all races, every age, and both sexes. In countries in which smallpox has been prevalent for generations it was, prior to the introduction of vaccination, a disease of early childhood, owing to the fact that practically all the adults would have previously passed through the disease. In vaccinated communities this incidence of the disease is no longer found to persist. Smallpox is not limited to any particular portion of the globe, although it is apt to be more severe in warm climates. It has usually been especially virulent on its first introduction into any country, as an instance of which may be cited an epidemic which occurred in Iceland in 1707-1709, from which about one-third of the total population died.

Seasonal prevalence. — In England and other temperate climates smallpox is apt to be most prevalent in spring, autumn, and winter, comparatively few cases being met with in the summer. MacCombie states that he has frequently noticed that in outbreaks commencing in autumn, there has been a sudden drop in June the following year, and that the lessened incidence prevailed during the summer months. But he does not consider it probable that this drop is mainly due, as has been suggested, to the more open-air habits of life in summer.

Mode of conveyance. — Smallpox infection may be either direct or indirect, and it has recently been shown by Mr. Power and others that the contagium may be carried for a considerable distance through the air from a smallpox hospital, especially at times when the latter contains a number of acute cases. Most frequently, however, a previously healthy person becomes infected through close contact with a patient suffering from the disease. Cases of smallpox must be considered as infectious from the earliest onset of the disease, although the danger is probably greater after the appearance of the eruption, and perhaps especially so when the

crusts are commencing to separate. The bodies of persons who have died of smallpox are also capable of conveying the disease, though it may be that actual contact is necessary in this case. Infection is also not unfrequently conveyed by articles of personal use, such as clothing, bedding, and the like, even after considerable intervals of time, during which they may have been stored, and outbreaks have occasionally occurred in paper-mills from the use of infected rags in the manufacture of paper. It is also possible that healthy persons, who have been in contact with the sick, may convey the disease to others by means of their clothing or hair.

Seasonal Curve of Smallpox Mortality (London), Mean of 40 Years.



Each division corresponds to 10 per cent above or below the mean annual mortality indicated by dotted line.

An individual is only to be considered as free from the liability to transmit variola "when every scab has fallen off and the skin lesions have all healed" (Medical Officers of Schools, Code of Rules).

Incubation.—The period which may elapse after exposure to infection, by which alone smallpox in the present day is contracted, and before any definite symptoms pointing to invasion of the system by the disease becomes obvious, has been variously estimated, but in the great majority of cases is found to be, as nearly as possible, twelve days. The Code enjoins an isolation for sixteen days after exposure to infection and thorough disinfection at the commencement of the period.

Symptoms and progress.—During the incubation stage of smallpox it is exceptional for any definite symptoms to present themselves, although occasionally the patient may complain of a feeling of languor and general malaise. The appearance of the typical eruption is preceded for about a couple of days by certain well-marked symptoms, commencing with a somewhat sudden and often rapid rise of temperature, ushered in with chills or actual rigors, or, in children, convulsions. In adults especially, heat and perspiration of the skin may be profuse, and anorexia, thirst, and constipation well marked, together with a feeling of nausea, or actual vomiting. In children constipation is liable to be replaced by diarrhœa. Symptoms pointing to invasion of the nervous system usually present themselves early in the progress of the disease, of which acute lumbar pain is at once the most typical and constant. Headache and aching of the limbs are often complained of, together with drowsiness, which may pass into stupor and coma. On the other hand, delirium not unfrequently supervenes, occasionally developing into a maniacal condition. The symptoms of this stage are severe in proportion to the severity of the attack which they usher in. Other things being equal, therefore, the higher the temperature, the more persistent the vomiting, the acuter the pain in the back, and the more pronounced the implication of the brain, the more quickly will the disease assume grave proportions, and the greater will be its intensity and the prospect of a fatal issue.

By about the third day these prodromal symptoms will attain their maximum, and the *eruption* typical of the disease appears. The rash commences as minute reddish papules, which are distinctly hard, giving a "shotty" sensation when the finger is passed over the skin. These are first found, and in greatest numbers, on those parts of the body which are ordinarily uncovered, more particularly the face, head, neck, and wrists. During the next two days the chest, abdomen, and upper and lower extremities become invaded, though to a less extent. The papules gradually enlarge, and in the course of two or three days become converted into vesicles. About three days later the vesicular contents, at first limpid, will have become purulent. The resulting pustule increases in size, and becomes surrounded by a dark red zone of inflammation, termed the "areola." The inflammation, together with the swelling of the underlying tissues due to inflammatory exudation, still further increases up to about the ninth day (eleventh day of the disease), or even a day or two later in the case of that portion of the eruption on the lower part of the trunk and extremities. When the

eruption is somewhat scanty, the separate pocks on the face remaining distinctly isolated from one another, the attack is said to be of the *discrete* variety, the papules in this form of the disease not unfrequently showing a crescentic arrangement in their grouping. If, on the other hand, the pocks are so numerous as to coalesce with one another, the disease is said to be of the *confluent* form. In certain specially severe cases, the so-called *hæmorrhagic smallpox*, the contents of the pocks at quite an early stage are found to be mixed with blood, while in a still severer form of the disease, *malignant smallpox*, minute punctiform hæmorrhages become visible at an early stage just beneath the surface of the skin, the patient probably dying collapsed before the appearance of the typical eruption.

Although most obvious on the skin, the rash of smallpox is by no means confined to the outer surface of the body. It not unfrequently develops to a considerable extent on the mucous membrane of the mouth, nose, and throat, and even that of the larynx and trachea, and of the conjunctiva.

Prodromal rashes. — The eruption typical of the disease is occasionally preceded for a day or two by rashes bearing somewhat of a resemblance to those which occur in measles and scarlet fever. This is not unfrequently so in smallpox which has been modified by antecedent vaccination. Again, in cases which eventually prove to be of severe type an abundant rash either of somewhat similar character or of a hæmorrhagic nature is apt to occur, more particularly on the lower portion of the abdomen, where it usually occupies an area between the umbilicus and the pubes similar in outline to an inverted triangle, and also to a less extent on the chest and loins.

Specially characteristic of the disease is the fact that on the first appearance of the eruption all the symptoms from which the patient will previously have been suffering become ameliorated. To so great a degree is this the case, that in the milder form of the disease the patient may believe himself to have recovered, and persist in going about his ordinary avocations. Owing to this fact the disease is often spread by the peregrinations of tramps from town to town.

Although in an ordinary attack of smallpox the typical symptoms will thus in large measure have disappeared on the outbreak of the eruption, this latter will itself in all probability cause some inconvenience to the patient, as will also soreness of the mouth and tongue, which are likely to be accompanied with ptyalism. Owing to the eruption affecting to some extent the upper part of the alimentary and respiratory tracts, the throat

becomes painful and the voice hoarse, while the patient is often troubled with a harsh cough. In severe cases laryngeal complications are usually present from an early stage.

The after course of the disease will vary considerably in accordance with the severity or reverse of the attack. In the mildest cases the vesicles never become really pustular, commencing to contract and dry up before this stage is reached. In such cases the temperature, which will have fallen almost or quite to normal on the appearance of the eruption, does not again appreciably rise, and the patient speedily becomes convalescent. Ordinarily, however, after a period of apparent convalescence extending to about the eighth or ninth day of the disease the maturation of the pustules is ushered in by a period of secondary fever, accompanied, it may be, by chills or rigors and a rise of temperature as high as, or even exceeding that reached at the commencement of the disease. The pulse is quickened, anorexia again presents itself, and the patient may become delirious. In the confluent form of the disease little or no appreciable remission of symptoms accompanies the appearance of the eruption, although the temperature may perhaps fall a degree or so. Almost immediately, however, it mounts again, and both febrile and nervous symptoms rapidly become aggravated, attaining their maximum severity at about the period of maturation of the pustules.

If the course of the *temperature* be noted in a typical attack of the disease, it will be found to rise rapidly during the stage of invasion, it may be to 104°, or even 106°. As previously stated, it usually falls to a considerable extent coincidently with the appearance of the eruption, although for the most part not descending quite to the normal level. As the contents of the vesicles become purulent the temperature once more rises to 102°, 103°, or even 104°, while in cases tending to a fatal termination this range may be exceeded by two or three degrees.

The *delirium*, which is so marked a symptom, more particularly of the severer cases, like the temperature, may show a temporary remission after the eruptive stage, reappearing once more, and even in a severer form, with the occurrence of the secondary fever. In some cases the patient, already delirious, may become violently maniacal.

The *pulse* becomes increased with the rise of fever, falls together with the temperature after the appearance of the eruption and again quickens with the period of secondary fever. *Respiration* also becomes more or less hurried in correspondence with similar variations

in the pulse rate. In severe confluent cases the breathing is apt to become shallow and laboured.

The *urine* is febrile in character. During the pustular stage of the disease the amount of urea excreted is markedly increased, and albuminuria has been found to occur in about one-third of the total number of cases. Hæmaturia is rare.

Thirst is a marked feature throughout, and in the milder forms of the disease *perspirations* persist from first to last, except in the case of children. In confluent smallpox, however, perspirations are exceptional, while *salivation* is a common and troublesome symptom. In such cases, on account of the *swollen condition of both mucous membrane and skin*, the mouth cannot be closed, while, owing to the swelling of the eyelids, it is difficult or impossible to open the eyes. The nose, ears, and lips also may become so enormously swollen as to render the patient unrecognisable, even to his relatives. The extremities in like manner are often so œdematous and painful that even the weight of the bed-clothes can hardly be endured.

Within three or four days from the commencement of the pustular phase of the eruption, by which time the secondary fever in favourable cases will have practically subsided, the pustules will either dry up, forming for the most part flattened, reddish-brown scales, or they become ruptured, their contents escape, and, drying up, dark-coloured, thick, adherent crusts result. Most typical of this stage is a peculiar *fetid odour*, which has been likened to the smell of mice, exhaled from the skin.

The swelling of the skin now subsiding, the features return more or less to their previous appearance, and during the third week of the disease the "crusts" commence to separate, but, owing to the occasional formation and separation of successive "crusts," the resulting sores may not be completely healed for another week or more.

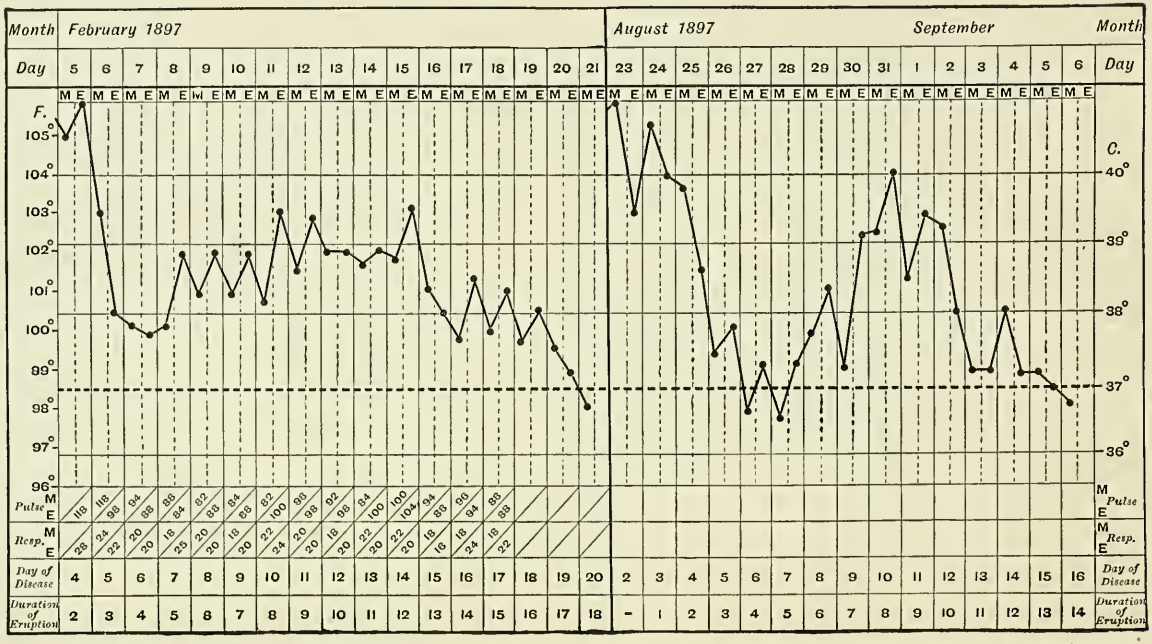
From this period onwards, in favourable cases, rapid progress towards convalescence may be expected, although even in the milder cases there is a possibility that certain complications and sequelæ may intervene.

Complications and sequelæ.—An attack of smallpox is liable to be followed by various sequelæ, whether the attack itself be mild or severe, although serious complications more commonly manifest themselves after the confluent form of the disease; of these perhaps the most common is *erysipelas*, particularly of the face and head, together with boils, and probably, later on, abscesses, both subcutaneous and deep-seated, which may attain a large size and heal with difficulty. *Otitis* and *conjunctivitis* may be met with,

Temperature Curves in Two Cases of Confluent Smallpox.

Male, æt. 11 Years—Unvaccinated.

Female, æt. 11 Years—Unvaccinated.



Illness began on the 2nd; papular rash appeared on the 4th inst.

Illness began on the 22nd; papular eruption appeared on the 24th.

Kindly furnished by Dr. Ricketts, Medical Superintendent, Smallpox Hospital Ships, Metropolitan Asylums Board (S.M.C.).

ophthalmia occasionally ensuing in consequence of the formation of pustules on the conjunctiva. These never occur on the cornea itself, although a form of ulceration which is apt to extend slowly from one side of the cornea to the other is occasionally observed.

Other possible complications include *bronchitis*, *broncho-pneumonia*, and *pleurisy ; paralysis of the extremities* or *bladder* has been observed.

As the result of the destruction of the cutis vera, which will be more or less extensive according to the amount of the original eruption, indelible *cicatrices* will be left ; the face specially, after a severe confluent attack, often remaining scarred and seamed in all directions. The ophthalmia, to which reference has already been made, may result in permanent blindness. Permanent alopecia only occurs after severe attacks, and chiefly in adults. Unless the follicles have been destroyed, regeneration of hair, which may have been shed during the course of the disease, takes place rapidly and abundantly after recovery.

Morbid anatomy and histology.—Except in severe hæmorrhagic cases, in which blood will be found effused into the substance of the solid viscera, and beneath the serous and mucous surfaces, no special appearances are likely to be observed on post-mortem examination.

Comparatively little is known as to the actual histological changes occurring in the skin in smallpox during the development of the eruption, there appearing to be no record of any continuous study of the minute anatomy of this disease. So far as can be judged from such examination as has been made of the microscopical structure of the skin at various stages of the eruption, there would appear to be a complete similarity with those observed during the eruption of vaccina, for an account of which reference may be made to the article dealing with this disease. The same article may also be consulted for a brief account of the bacteriology of these maladies.

Modified Smallpox or Varioloid is that form of the disease which is met with in persons who, at some time previous to their attack, have been vaccinated, but in whom the protection afforded by the operation has been insufficient, either from the vaccination having been imperfectly performed in the first instance, or because its effect has diminished through lapse of time.

No definite rule can be laid down as to the extent to which any one symptom or set of symptoms, are likely to be modified as the result of previous vaccination, but for the most part the case resembles a mild form of the discrete variety. Thus the disease may

be exceedingly mild from the commencement, and the eruption may be absent or be limited to the appearance of a few papules on the face or hands. Or the attack may commence with fairly high fever, generally, however, of short duration, accompanied by severe headache, lumbar pain and vomiting, only to abort soon after, or even before, the appearance of the eruption. If an eruption does present itself it usually does not develop beyond the vesicular or possibly the papular stage, and secondary fever, if it supervenes, is comparatively slight. It is in cases of modified smallpox that generalised prodromal rashes resembling those of measles or scarlet fever are most often observed. It is rare for a case of modified smallpox to have a fatal termination.

Diagnosis.—The diseases from which smallpox is most likely to be with difficulty distinguished are:—

In the initial stages, measles, scarlet fever, syphilis, and the rashes which occasionally appear as the result of the administration of antitoxin or the bromides.

In the later stages the discrete or modified variety may simulate chicken-pox or acne.

If an initial rash should present a difficulty, the appearance of the typical rash will probably render the diagnosis certain. The diagnosis of modified smallpox from chicken-pox, however, deserves more detailed description.

Differential diagnosis of modified smallpox and chicken-pox.—A well-developed attack of natural smallpox could hardly be mistaken for varicella, but in respect to the modified disease, especially with a sparse eruption, the diagnosis may present considerable difficulty. Careful attention to the following points, however, will usually serve to dispel any doubt as to the nature of the case.

(*a*) In modified smallpox the eruption, however scanty, is almost invariably preceded by severe febrile symptoms of two days' duration. In varicella this *prodromal illness*, except very occasionally in adults, is wanting. The rash is usually the first sign, preceded possibly for a few hours by a feeling of malaise.

(*b*) In variola the *eruption*, whatever its amount, will all be visible within thirty-six to forty-eight hours of its first appearance; but in varicella the eruption usually comes out in distinct crops, extending over a period of three to five days, or more.

(*c*) The *temperature* in variola falls rapidly, immediately the eruption appears, whereas in varicella each crop is commonly attended with a fresh rise of temperature.

(*d*) Although in most cases of modified smallpox the vesicles

are not fully formed until the third or fourth day of the rash, instances are occasionally seen in which some of the papules show an attempt at *vesiculation* within twenty-four hours of their first appearance. The presence, however, of one single, well-developed, tense vesicle by the end of the first day is practically sufficient to exclude variola, though common enough in varicella, especially on the trunk and thighs.

(*e*) The vesicle of variola usually shows more induration of its base, and collapses less readily when pricked than does the vesicle of varicella.

(*f*) In variola the pocks situated within a circumscribed area, being for the most part of the same age, attain coincidently the same degree of development, whereas in varicella, owing to the eruption commonly appearing in successive crops, pocks in all stages of development—from papule to scab—may often be detected side by side.

(*g*) The relative *distribution of the eruption* varies; in variola it is apt to be more copious on the face and extremities, whereas in varicella it is usually most prevalent on the trunk, upper arms, and thighs.

Valuable confirmatory evidence may be gleaned from a history of exposure and infection, or by the discovery of scars indicative of vaccination, or of previous varicella. The presence of the latter is almost sufficient to exclude chicken-pox, so excessively rare is a second attack, while in a child the presence of good vaccination scars will similarly tend to exclude smallpox. Chicken-pox in an adult is probably as rare as smallpox in a well-vaccinated child. Additional evidence may be gained by vaccinating the patient and observing what result, if any, follows the operation.

Treatment.—To Sydenham we owe the indications for the treatment of smallpox, which is in use at the present day. He first insisted on the absolute necessity of keeping the patient cool, while avoiding chills, this being attained by thorough ventilation of the bed-chamber, which should at the same time be kept at as equable a temperature (about 60° F.) as possible.

No medicinal treatment appears to be of avail in cutting short the course of the disease, although the various symptoms and complications should receive appropriate treatment as they arise. The comfort of the patient will be increased by the free administration of cooling drinks, such as lemonade, soda-water and milk, or toast and water, while at the same time some saline or acid medicine may be given. If the mouth be sore some relief may be obtained by allowing the patient to

suck black-currant jelly, or by painting it with a solution of boro-glyceride, while if there be much discharge from the nose and throat, a solution of some mild antiseptic, such as boracic acid or permanganate of potash, will be found of service as a wash. If either constipation or diarrhœa be present, they must be treated with suitable remedies. The drug most likely to be of service in this disease is opium, since it is valuable both for the relief of the delirium and of the severe pain which is commonly present during the period of invasion. It is equally serviceable during the secondary phase of the disease. In severe cases the tendency to collapse should be combated by the administration of ammonia, and of alcoholic stimulants, such as brandy or champagne. The patient should be placed on the ordinary fever diet, consisting for the most part of milk and slops. Even in the milder cases of the disease much discomfort is liable to be caused by swelling and irritation of the skin, which may be considerably relieved by frequent sponging with tepid water, followed by inunction of the skin with carbolised oil or vaseline. The eyes should receive particular attention, being carefully sponged at frequent intervals, whilst instillation of a weak solution of nitrate of silver (gr. i. to water ℥vi.) will be advisable if there be any tendency to inflammation of the conjunctiva.

From the earliest times innumerable plans have been suggested for the prevention of the pitting of the skin, which, especially after recovery from severe attacks of the disease, is liable to cause great disfigurement. It is, however, very doubtful whether such pitting can be prevented by any means at our command;—that perhaps which is most likely to have the desired effect being the evacuation of the contents of the pock as soon as the presence of fluid can be detected. During convalescence it is of the utmost importance that the patient's strength should be supported by the administration of tonic remedies together with stimulants and a generous diet.

The success which has already attended the method of serum-therapy, more particularly in diphtheria, has led to the hope that a similar method may presently be available for the treatment of smallpox, but thus far the object in view has not been attained.

As regards the *prevention* of this disease we have in efficient vaccination and revaccination a prophylactic method of the utmost value. This subject, however, will be treated of in a separate section.

Smallpox Inoculation.—By the term inoculation is meant the purposeful implantation of smallpox virus beneath the surface of the skin in the same manner in which vaccination is now carried out.

The origin of this procedure is unknown, although undoubtedly it has been practised by the Chinese and Hindoos for centuries. From them it extended westwards into European Turkey, whence it was brought to England in 1721 by Lady Mary Wortley Montagu, the wife of the then English Ambassador to the Ottoman Court.

The insertion of smallpox lymph beneath the skin was followed by a series of events very similar to those arising from vaccination. The mature vesicle, however, had a more irregular outline than the vaccine vesicle, and was usually surrounded by a number of tiny secondary vesicles, many of which eventually merged into the primary one. Occasionally, as in the mild inoculations carried out at the commencement of the present century by two brothers of the name of Sutton and by Adams, no other result followed than the appearance of the vesicle, or vesicles, at the site of operation. Oftener, however, between the eighth and tenth days after the inoculation a general eruption followed, which might be limited to a few vesicles on the forehead, or might result in a copious outbreak involving almost every portion of the body. During the last century the risk of any individual contracting smallpox was felt to be so great that people, while still in good health, were ready to run the risk of purposely contracting the disease, in what was usually under these circumstances a mild form, in order to avoid the grave danger to life which was inseparable from the disease contracted in the ordinary manner. The process of inoculation was certainly of value to those individuals on whom it was carried out, since, although a certain number of these contracted the disease in severe form and even died of it, yet the death-rate was in all probability no more than one in three hundred of those operated on, whereas that of ordinary smallpox was apt to be as high as fifty per cent. Although this was so, the practice of inoculation, by carrying smallpox into remote districts where otherwise it might not have penetrated, and owing to the fact that inoculated smallpox, even in its mildest form, was apparently as contagious as the ordinary disease, the actual amount of smallpox in the country, during the period succeeding the introduction of inoculation, was probably much higher than otherwise would have been the case. At the present day inoculation has only an historic interest, seeing that since the Vaccination Act of 1840 came into operation the intentional communication of smallpox from person to person in this manner has been a penal offence.

S. Monckton Copeman.

VACCINIA

Syn. Cow-pox

Vaccination

Vaccinia is, in the human subject, a specific communicable disorder, arising, except in very rare instances, from the accidental or intentional inoculation of an individual with vaccine lymph. The disease is characterised by the appearance of a local eruption, passing through the stages of papule, vesicle, and pustule, associated with more or less constitutional disturbance.

Similar symptoms are produced whether the lymph employed for inoculation has been derived from the vesicles of a previous case in the human being, or from the eruptive vesicles of a disease of bovine animals called cow-pox. Such inoculation process, whichever way induced, is known as *vaccination.* This name was originally devised in accordance with the terminology of Jenner, who wrote of the disorder under the title of Variolæ vaccinæ. In this manner he gave expression to his belief that the malady commonly known as cow-pox was in reality nothing more nor less than smallpox of the cow.

Cow-pox in the cow.—For a description of cow-pox in typical form, as it was known to Jenner and his contemporaries, it is necessary to consult the writings of the early part of the century, at which period the disorder was much more rife than at the present day. According to observers such as Bryce and Ceely, this affection, when once set going in a herd, tends to spread with considerable rapidity, the "matter" of the vesicles which appear on the teats and udders being carried by the hands of the milkers from one cow to another. If the material happen to come in contact with an abrasion of the skin of the milker's hand, such person is apt to become infected with the disease. When the ailment is communicated in this manner, it is termed *casual cow-pox*, to distinguish it from that form which is intentionally propagated by vaccination, under which circumstances the affection is less virulent than when communicated in the former way.

Inoculated cow-pox (vaccination) in man.—In the cow-pox induced by inoculation the appearances which present themselves differ in some respects from those occurring in the casual disease.

Thus about the third day after the insertion of vaccine lymph a small inflamed spot may be observed at the point where the vaccination was performed. Next day this spot appears more florid, and on passing the point of the finger over it, a certain degree of hardness and swelling is perceptible. By the fifth day a small pale vesicle occupies the spot where the inflammation began. This vesicle has a milky-white colour without any inflammatory zone around it; it is depressed in the centre, its edges being distinctly elevated. For the next two days the vesicle increases in size, assuming a circular form if the vaccination was performed by a puncture; if done by an incision, an oval shape. But in both cases, the margin is regular and well defined. About the eighth day an inflammatory zone (of a bright red colour, termed the areola) begins to appear around the base of the vesicle. This increases for two, or perhaps three, days more, by which time it may extend for about a couple of inches from the vesicle. The vesicle still retains its concave appearance, and a crust of a brownish colour will have commenced to form in the centre. About the eleventh day the vesicle has attained its greatest magnitude, and the surrounding inflammation begins to abate. The fluid in the vesicle, which before was thin and transparent, is now more viscid and somewhat turbid. After this period the whole becomes quickly converted into a smooth, shining, dry crust of a dark-brownish or red colour. This crust, unless forcibly removed, will adhere for a week or more, and then fall off, leaving the skin beneath apparently sound, but livid for a time, and more or less permanently scarred.

Relationship of Variola and Vaccinia.—As evidence of a definite relationship between smallpox and cow-pox, it may be mentioned that whereas, prior to the introduction of vaccination, epidemics of these disorders frequently occurred in relation to one another, the so-called "natural" cow-pox has now in great measure disappeared. There is, moreover, no appreciable difference in the anatomical characters or in the progress of the eruption in the two affections, both of which also appear to be mutually protective against each other. But of far greater importance in this connection are the results obtained by numerous observers, who in various parts of the world, and almost from the time of Jenner onwards, have set themselves the task of attempting, by experimental methods, to solve the problem of the true relationship of variola to vaccinia. As the outcome of this work it may now be definitely stated that smallpox lymph, by passing through

the system of the calf, can be so altered in character as to become deprived of its power of causing a generalised eruption, while inducing at the site of inoculation a vesicle indistinguishable from a typical vaccine vesicle; and more important still, that when transferred again to man, it has by such treatment completely lost its former infectious character. Such being the case, it may fairly be asserted that cow-pox—or rather that artificially inoculated form of the disease which we term vaccinia—is nothing more nor less than variola modified by transmission through the bovine animal.

Histology.—During the evolution of the local changes which result from the insertion of vaccine lymph beneath the surface of the skin, it is possible to recognise three more or less definite stages of papule, vesicle, and pustule. The same statement holds good with reference to the eruption of smallpox, whether this be local, *i.e.* due to inoculation of the virus, or general, as the result of infection.

In each instance the appearance of the first or *papular* stage is brought about by inflammatory reaction, causing an increase of intercellular fluid, together with concomitant increase in volume and number of epithelial cells, of the rete Malpighii more particularly. The papule gradually becomes enlarged by a circumferential extension of the same process, and, owing to further changes in the cells first affected, vacuoles arise in the central portion of the papule, by the extension of which this ultimately becomes a vesicle. The *vesicle* is a multilocular structure, the dissepiments, by means of which its interior is divided up, being formed from the thinned and extended remains of the original epithelial cells. Owing to the fact that the process of vacuolation for a time increases more extensively at the advancing edge of the vesicle, the central portion remains somewhat less elevated, thus giving rise to the appearance termed umbilication. At a quite early stage of the process an outflow of leucocytes takes place towards the point of injury. These, by the increase in their numbers, eventually transform the originally clear, inflammatory exudation into a purulent fluid. The vesicle is said now to have become converted into a *pustule*. By the thinning and ultimate rupture of its trabeculæ, the pustule finally becomes unilocular. The turbid fluid contained in it now gradually dries up, and, together with the necrosed remains of epidermal cells, takes part in the formation of the *crust*, which, under the microscope, appears as a homogeneous mass very deeply coloured by the ordinary bacteriological stains. Meanwhile a regeneration goes on underneath the crust, the new epidermis being formed from an ingrowth from the

surrounding stratum lucidum. The extent to which the cutis vera has been involved determines the depth of the resulting scar.

Bacteriology.—There is much evidence to prove that the results following on the process of vaccination are due to a specific contagium, and, moreover, that the particular micro-organism concerned is capable of existing, during one period of its life cycle, in a resting or spore form, which is more resistant to the germicidal effects of glycerine than is the case with non-sporing microbes. Up to the present, however, no satisfactory method has been devised by which the micro-organism of vaccinia can be unfailingly cultivated on artificial media while still retaining its specific properties.

History of vaccination.—Rather more than a century ago, in the summer of the year 1798, there was published a pamphlet entitled "An Inquiry into the Causes and Effects of the Variolæ Vacciniæ, etc." This was the work of Edward Jenner, a country medical practitioner living at Berkeley, in the Vale of Gloucester, and in it the author set out the results of certain investigations on the possibility of affording protection against human small-pox by the intentional inoculation of a disease of cattle called cow-pox.

Many years before, while apprenticed to a medical man at Sodbury, near Bristol, Jenner's attention had first become directed to a belief, widely prevalent in Gloucestershire during the latter half of the eighteenth century, that those persons who in the course of their employment on dairy farms happened to contract cow-pox were thereby protected from a subsequent attack of smallpox. In particular, his interest was aroused by a casual remark made by a young countrywoman, who happened to come to the surgery one day for advice, and who, on hearing mention made of smallpox, immediately volunteered the statement that she could not take the disease as she had had cow-pox.

On coming up to London in 1770 to finish his medical education, Jenner became a pupil of John Hunter, with whom he frequently discussed the question of the possibility of obtaining protection against smallpox. On his return to his native village of Berkeley in 1773 to practice as a medical man he took every opportunity of talking over and investigating the matter, but it was not until May 1796 that he commenced actual experiments. Jenner's first case of vaccination was that of a boy, eight years of age, whom he inoculated in the arm with cow-pox matter taken from a sore on the hand of a dairymaid, who, in turn, had become infected with the disease from milking cows suffering from cow-pox.

It was apparently not until 1798 that he made his first attempt to carry on a strain of lymph from arm to arm. In the spring of this year he inoculated a child with matter taken directly from the nipple of a cow; and from the resulting vesicle on the arm of this child first operated on, he inoculated, or, as it may now be more correctly termed, "vaccinated," another. From this child several others were vaccinated; from one of these a fourth remove was carried out successfully, and finally a fifth. Four of these children were subsequently inoculated with small-pox—the "variolous test"—without result.

Extent of the protection afforded by vaccination.—As the result of prolonged investigation of the effect of vaccination in reducing the prevalence of, and mortality from, smallpox the following conclusions were arrived at by the majority of the members of the Royal Commission on Vaccination, whose final report was published in 1896.

1. That it diminishes the liability to be attacked by the disease.

2. That it modifies the character of the disease and renders it (*a*) less fatal, and (*b*) of a milder or less severe type.

3. That the protection it affords against attacks of the disease is greatest during the years immediately succeeding the operation of vaccination. It is impossible to fix with precision the length of this period of highest protection. Though not in all cases the same, if a period is to be fixed, it might, we think, fairly be said to cover in general a period of nine or ten years.

4. That after the lapse of the period of highest protective potency, the efficacy of vaccination to protect against attack rapidly diminishes, but that it is still considerable in the next quinquennium, and possibly never altogether ceases.

5. That its power to modify the character of the disease is also greatest in the period in which its power to protect from attack is greatest, but that its power thus to modify the disease does not diminish as rapidly as its protective influence against attacks, and its efficacy, during the later periods of life, to modify the disease is still very considerable.

6. That re-vaccination restores the protection which lapse of time has diminished, but the evidence shows that this protection again diminishes, and that, to ensure the highest degree of protection which vaccination can give, the operation should be at intervals repeated.

7. That the beneficial effects of vaccination are most experienced by those in whose case it has been most thorough. We think it may fairly be concluded that where the vaccine matter is inserted in three or four places, it is more effectual than when introduced into one or two

places only, and that if the vaccination marks are of an area of half a square inch, they indicate a better state of protection than if their area be at all considerably below this.

Re-vaccination.—The protection afforded by a primary vaccination tends gradually to diminish and eventually to disappear more or less completely with the lapse of time. In consequence, it is desirable that the operation should be repeated at the age of from seven to ten years, and thereafter, if it be possible, at intervals during later life. The Report of the Royal Commission on Vaccination thus summarises the evidence as to the value of such additional procedure.

Where re-vaccinated persons were attacked by, or died from, smallpox, the re-vaccination had for the most part been performed a considerable number of years before the attack. There were very few cases where a short period only had elapsed between the re-vaccination and the attack of smallpox. This seems to show that it is of importance in the case of any persons specially exposed to the risk of contagion that they should be re-vaccinated, and that in the case even of those who have been twice re-vaccinated with success, if a long interval since the last operation has elapsed, the operation should be repeated for a third, and even for a fourth time.

It not unfrequently happens that in the case of a re-vaccination the process runs a somewhat different course to that witnessed in a typical primary vaccination. Owing probably in large measure to the age of the patient, and the consequent difficulty in keeping the vaccinated arm completely at rest, somewhat extensive inflammation of the skin is apt to ensue. This occasionally may be further complicated, it may be with lymphangitis, swelling, and even suppuration of the axillary glands and general malaise. In a successful vaccination, papules make their appearance about the third to the fifth day at the site of the operation. The papules may or may not develop further into vesicles and pustules. Occasionally a second or later vaccination appears to fail altogether, but as pointed out by the Royal Commission, it is advisable, as in the case of a primary vaccination, to make further attempts before concluding that the individual is really insusceptible.

Alleged injurious effects of vaccination.—In a certain small proportion of cases the operation of vaccination is apt to be followed after a longer or shorter interval by various complications, of which by far the most important are those of an inflammatory nature, which "constitute the danger of any local lesion of the

skin" (Acland). Those most liable to be met with include erysipelas, septicæmia, and pyæmia, abscess, and ulceration, simple or gangrenous. Dr. Acland has shown that, approximately, 60 per cent of all cases of vaccinal injury in this country are probably due to some form of inflammation, erysipelas being the most important and of the most frequent occurrence.

There is unfortunately some reason for the assertion that syphilis has, on occasion, been in-vaccinated, although the number of authenticated cases are extremely few. Seeing, however, that the use of calf lymph has now become practically universal, the possibility of such untoward occurrence in the future may be disregarded, seeing that the calf is not capable of contracting this disease.

Tubercle in its various forms and leprosy have also been included in the list of possible complications of vaccination, though without any sufficient proof. The employment of calf lymph treated with glycerine after the manner first advocated by the writer, and now officially adopted by the Government, will obviate any such danger, for even if bacilli of tubercle were by chance present in the lymph material when collected, it has been found that they are quite unable to survive the prolonged action of a fifty per cent solution of glycerine in water. Leprosy is not communicable to the calf.

Certain skin diseases, such as eczema and impetigo, sometimes appear during the course of, or shortly after, vaccination; but no direct connection has been proved to exist between the operation and the occurrence of these disorders.

In section 434 of the Final Report of the Royal Commission on Vaccination the extent to which other inoculable diseases are liable to complicate vaccination are thus summed up:—

"A careful examination of the facts which have been brought under our notice has enabled us to arrive at the conclusion that although some of the dangers said to attend vaccination are undoubtedly real and not inconsiderable in gross amount, yet when considered in relation to the extent of vaccination work done they are insignificant. There is reason further to believe that they are diminishing under the better precautions of the present day, and with the addition of the future precautions which experience suggests will do so still more in the future."

The nature of the precautions most necessary to be observed will be considered in a separate section.

Practice of Vaccination

Collection and storage of vaccine lymph.—Hitherto the use of arm-to-arm human lymph has been insisted on in this country in the case of all vaccinations performed at public stations, for the reason that until recently this was the only method by which lymph stocks could be perpetuated and the greatest possible purity of the lymph ensured. In view, however, of the recommendations of the Royal Commission, and under the provisions of the Vaccination Act of 1898, this method will, as regards public vaccinations, be discontinued in the future in favour of the use of calf lymph, partly with the object of diminishing the very remote possibility of the conveyance of syphilitic infection by the operation. By this change of method also the necessity for opening vaccination vesicles, and thereby of affording opportunity for other local infections, will in large measure be avoided.

If human lymph be required the vesicles should be opened by a number of minute punctures, which must be made on its surface and not around its base. The object of such multiple puncture is to open the various cell-spaces in which the lymph is contained; that of puncturing on the surface, rather than around the base, is to avoid any admixture with blood. Lymph soon collects in droplets at the points of incision, and may be removed on a lancet, or if required for use at a distance, may be taken up into capillary tubes.

To fill a capillary tube it should be held in a more or less horizontal position and one end applied to a drop of lymph exuding from a vesicle which has been punctured, when the lymph immediately enters by capillary attraction. No more should be allowed to enter than is sufficient to fill the tube from one-half to two-thirds of its length. *The tube is sealed* by applying the empty end to the flame of a candle or spirit-lamp, as much as possible of the contained air having been previously driven out by momentarily plunging into the flame the whole of that portion of the tube in which there is no lymph. By this means, as soon as the extremity is sealed, the column of lymph is driven by atmospheric pressure towards the end first closed, and the point at which the lymph found entrance can then be sealed in the flame in the same manner as was the other.

The method, formerly employed, of storing lymph in the dried condition on ivory points is not to be recommended.

Glycerinated lymph.—The almost universal occurrence of

extraneous microbes in vaccine lymph, and the chance of addition, during or after vaccination, of pathogenetic micro-organisms by agency of careless people, whether vaccinators or persons having charge of infants, have been advanced as reasons for avoiding vaccination, on the ground of the possible harmfulness of micro-organisms liable to be introduced into the lymph at the time of the operation, or subsequently in the course of the evolution of the resulting pock. This argument, however, so far as the microbes usually intimately associated with lymph are concerned, loses whatever weight it may have had, since the writer has shown that by thoroughly incorporating the lymph or vesicle pulp with a sterilised fifty per cent solution in water of chemically pure glycerine, and afterwards storing the mixture for some weeks prior to use, protected from light and air, all the ordinary saprophytes found associated with lymph are eventually destroyed. This result is proved by the fact that no growth arises in any of the ordinary culture media inoculated with such glycerinated lymph. This statement applies equally to the bacillus of tubercle and to the streptococcus of erysipelas, should these microbes have been originally present in, or have been added experimentally to, the lymph. The employment of glycerinated calf lymph is now officially recognised by the Government, the lymph being issued, free of charge, to public vaccinators in any quantity required.

Insertion of vaccine lymph.—This process may be carried out either by scarification, by puncture, or by multiple superficial incisions. Doubtless the individual operator will attain the greatest measure of success by employing the method with which he is most familiar; but there can be little doubt that the method of insertion by scarification is the one that is most satisfactory, more particularly if the lymph has been preserved with glycerine.

The mode of operation is briefly as follows:—The arm should, if possible, be first washed with soap and warm water, and afterwards carefully dried with a soft towel, gentle friction being employed so as to cause a certain amount of distension of the cutaneous capillaries. Drops of lymph, corresponding in number to that of the vesicles which it is required to produce, are then to be placed on the surface of the arm, and the skin put slightly on the stretch with the fingers of the left hand. Next, the skin is scarified by a system of "cross-hatching," through the drops of lymph, by means of whatsoever instrument may be preferred, care being taken not to place the insertions too closely together, lest the vitality of the tissues between them be injured.

An ordinary bleeding lancet, the point of which has been slightly blunted, or a spear-pointed surgical needle, are both very efficient for the purpose of scarification. Complicated instruments should be avoided, since, as a rule, it is difficult to keep them thoroughly clean. The special advantage of a needle is that a new one can be employed on every occasion. If a lancet or like instrument be employed, it is essential that it should be boiled or otherwise sterilised immediately before use.

The strictest aseptic precautions should also be observed in the immediate and subsequent treatment of the vaccinated area. With the object of obtaining this result, the scarified spots should be protected either by a dressing of boracic lint, or by being covered over with a layer of collodion or other protective tissue, which, if possible, should be allowed to remain undisturbed for at least a week. On inspection, which, by the regulations of the Local Government Board, is now required to be done in public vaccinations between the sixth and fourteenth day, the dressing should be renewed. If, by any chance, the vesicles should have become ruptured, the use of a pad of absorbent wool (or wood-wool) may be advisable; otherwise a couple of layers of boracic lint, retained in position by means of strapping, will suffice. This second dressing should be left on the arm until the "crusts," to which the vesicles will have given rise, have separated of their own accord, and the regenerated skin-area beneath is soundly healed.

S. Monckton Copeman.

MUMPS

Syn. Epidemic Parotitis, Infectious Parotitis

Mumps is an acute infectious disease, of which the characteristic feature is inflammation of the salivary glands.

Etiology.—It has been known to occur in all parts of the civilised world, chiefly in localised outbreaks, often limited to the inhabitants of particular institutions, such as schools or barracks. Occasionally its prevalence is more widely spread.

Of recorded epidemics, the largest number have arisen during the winter and spring. While the disease is met with at all periods

of life, it is most common between the ages of five and fifteen. Both sexes are equally liable to be attacked. The infection is nearly always spread directly from the sick to the healthy, but it may be conveyed by a third person or infected articles.

The **incubation period** is three weeks; it may be as short as fourteen, and as long as twenty-five days. The Medical Officers of Schools Association recommend twenty-four days' quarantine, dating from exposure to infection, if disinfection have been carried out at the commencement.

Symptoms.—In some cases the attack is ushered in by prodromal symptoms—slight sore throat, fever, chilliness, malaise, headache, and vomiting. In others the illness begins with the signs of parotitis. There is pain behind one angle of the jaw, which is quickly followed by swelling of the parotid gland. For two or three days the swelling increases till it extends forwards on the cheek and downwards to the neck; it is elastic and very painful. The skin over it may be inflamed. After a day or two the swelling subsides, and disappears in three or four days.

Often the affection is not confined to one parotid gland. The submaxillary and sublingual salivary glands on the same side become involved, and, usually after an interval of a few days, the salivary glands of the opposite side. When, as occasionally happens, both sides are simultaneously affected, the swelling on each side of and below the jaw gives rise to deformity so great as to render the patient's features quite unrecognisable.

At the commencement of the attack the temperature may rise to 102° or 103° F., and for a day or two remains at about this height; then it gradually falls to the normal, to rise again when the second gland is affected. In some cases there is no pyrexia. The pulse-rate is slightly increased. In severe cases there may be delirium. During the period of parotid inflammation the patient experiences great pain on all attempts at swallowing or speaking, and sometimes he can hardly separate his teeth without discomfort. The salivary secretion is diminished and the mouth becomes dry. Occasionally the gums are swollen. In addition to the salivary glands the cervical lymph glands may become inflamed.

The disease assumes various forms. The swelling of the parotid glands may be trivial. In rare instances the submaxillary salivary glands alone are affected; or the salivary glands escape altogether, and the cervical lymph glands only are inflamed. Lastly, orchitis may be the only local manifestation of mumps.

It is very rare for the parotitis to suppurate or to become chronic.

Complications.—In a considerable proportion of males, usually adults (33 per cent, Laveran), *orchitis* follows an attack of mumps. This event generally occurs in from six to eight days after the parotitis, but it may be delayed for three weeks. In rare instances it precedes the inflammation of the salivary glands. The body of the testis, at times also the epididymis, becomes painful and swollen, attaining a considerable size. The scrotum may be red and œdematous. Even in slight cases pain may be felt extending up the cord into the abdomen. Occasionally the orchitis is attended by severe constitutional symptoms—pyrexia (102° to 105° F.), delirium, vomiting and diarrhœa, prostration, and infrequent pulse. The orchitis lasts four or five days, and is as a rule one-sided. It is followed by atrophy of the testis in about 70 per cent of the cases (Laveran): suppuration is rare. In the adult female also the sexual organs may be affected, but not so commonly as in the male; so that there is ovarian tenderness, inflammation of the external genitals, and mastitis.

Other complications are exceptional, but some of them are serious. Least uncommon are *ear-complications*. These may either accompany or follow an attack of mumps. There may be deafness, tinnitus aurium, vertigo and nausea depending upon inflammation of the internal ear. The deafness may become permanent, but is rarely double. In other cases there is otitis media. With respect to the *nervous system*, three classes of cases have been recorded: one in which the symptoms point to meningitis; a second in which they seem to depend on the blocking of a cerebral vessel (aphasia, hemiplegia, etc.); and a third where they are due to peripheral neuritis.

Amongst very rare complications may be mentioned—insanity, inflammation of the lachrymal gland (with orbital pain and swollen eyelids), jaundice, œdema glottidis, bronchitis, endocarditis, arthritis, nephritis, urethritis and prostatitis, and certain skin eruptions.

Pathology and morbid anatomy.—Mumps is most probably caused by a micro-organism, which, however, has not yet been identified, that reaches the glands *viâ* the ducts, and induces an inflammation which is chiefly interstitial.

Relapses and **second attacks** are uncommon. Catin, in an epidemic of 157 cases, met with 2 relapses and 9 second attacks.

The patient is infectious for two or three days before the parotid swelling arises, and the aforesaid authorities advise an isolation of the patient for "not less than three weeks from the

commencement—provided that one clear week has elapsed since the subsidence of the swelling."

Diagnosis.—The two conditions with which mumps is most often confounded are diphtheria and enlargement of the parotid gland due to other causes.

It is the extreme enlargement of the cervical glands present in some cases of diphtheria which occasions the error. Inspection of the fauces will settle the case. The parotid glands are unaffected in diphtheria.

Inflammatory enlargement of the parotids sometimes complicates other diseases, especially enteric fever and various abdominal and pelvic disorders. It then often results in suppuration.

Prognosis.—Mumps is very rarely fatal. The serious, though unusual, nervous complications mentioned above nearly always occur in cases where the testis has become involved.

Treatment.—To the painful parotid glands hot fomentations with glycerine and belladonna, or laudanum, should be applied. In many cases of orchitis the same treatment is applicable, but in others ice affords more relief. The diet should be such as the patient can take.

It is most important to bear in mind that orchitis may be induced by allowing the patient to get up and resume his ordinary duties too early. Hence caution should be exercised, and the male patient kept in bed for eight or nine days, and in his room for several days longer.

E. W. Goodall.

WHOOPING-COUGH

Syn. Chin-Cough, Pertussis

An acute specific disease—distinguished by general catarrh of the respiratory tract, with accompanying nervous phenomena, of which by far the most important is the characteristic laryngeal spasm. It is very infectious, and one attack usually affords complete protection from a second for the rest of life.

Bacteriology.—It is generally recognised that the contagium must be a living organism, and several different forms have been described, but the real one has not yet been isolated with certainty.

Present opinion appears to be in favour of that found by Koplick (and possibly previously by Afanasieff), who has isolated small bacilli from the mucus discharged at the end of a paroxysm, which he found to be present in thirteen out of sixteen cases examined. He describes them as very minute rods with rounded ends, which sometimes look like diplococci on account of the ends being the more deeply stained.

Whatever may prove ultimately to be the specific organism, there can be but little doubt that it causes an inflammation of the mucous membrane of the larynx and trachea, and that the toxin which it manufactures has a special influence on the centres of the pneumogastric and superior laryngeal nerves.

Infection, how spread.—From the above it will be seen that the infection is contained in the expectorated mucus. By this means the disease is frequently spread through the medium of clothes, bedding, curtains, etc., as is the case with scarlet fever, though how long the virus may remain active in such circumstances is very doubtful. From outbreaks recorded as having taken place on board ship, the fomites would appear capable of conveying infection for several weeks. By the same means individuals, themselves unaffected, may convey the complaint.

It may perhaps also be spread directly by the breath, but if so, the infection does not apparently spread very widely—as it is a matter of common experience to those connected with children's hospitals that the tendency for the disease to extend to the surrounding beds is but slight, when a case has been admitted accidentally into the wards.

Duration of infectivity.—A patient is infectious from the very commencement of the catarrhal stage, but for how long a time after has not been settled; probably there is but little danger six weeks after the onset of symptoms, even though the paroxysmal cough may not have entirely disappeared.

In the 4th edition of *A Code of Rules for the Prevention of Infectious and Contagious Diseases*, issued by the Medical Officers of Schools Association, the answer to the question when a patient can be considered as *free from infection* is laid down as "in not less than five weeks from the commencement of the whooping, and provided that the characteristic spasmodic cough and the whooping have ceased for at least two weeks," and "provided patient and clothes have been disinfected."

In the same work, twenty-one days from the date of exposure to infection is given as the proper period of **quarantine**, with a similar

proviso that disinfection has been carried out at the commencement.

Predisposing causes.—The disease, as already stated, is extremely infectious, and persons of all ages are liable to be attacked. The great majority of cases occur between the ages of one and ten years, a period which includes the time at which most children are first exposed to the infection. A good many infants of under one year of age suffer, and with them it is nearly always a serious and often a fatal disease. With adults and old people it is troublesome but hardly ever dangerous. Statistics show that girls are slightly more susceptible than boys.

An attack of measles appears to render an individual unduly susceptible to invasion by the virus of whooping-cough, at any rate in this country there is a very general belief that there is some close connection in this respect between the two diseases. No other factor seems to have a direct bearing on predisposition. Ill-nourished children and those that are rickety or unusually nervous make bad subjects, as they appear to be far less able to resist the pulmonary and other complications which so frequently arise.

Epidemics appear to be most prevalent during the late autumn, winter, and early spring months; certainly those that suffer during this period of the year are far less likely to get well quickly than those who have it during the warmer months.

The **period of incubation** is difficult to ascertain with precision, and cannot be quite definitely stated. Thirteen days was found by Dr. Murchison in one case to be the exact period (*Trans. Clin. Soc.* vol. xi. p. 243 *et seq*), and some other observers have confirmed this. It probably varies, however, in different individuals from four or five to eighteen days, or even longer.

Clinical history.—Incubation over, the active phase of the disease sets in, and this may be conveniently divided into three stages: (1) prodromal; (2) paroxysmal; and (3) that of defervescence. Between the first and second the distinction is fairly sharp, but the latter usually passes so gradually into the last as to make it impossible to say exactly where the one ends and the other begins.

Prodromal stage.—The first or prodromal stage generally lasts about a week or ten days. It is often acute, having all the characters of a severe cold, with considerable disturbance of the respiratory tract, accompanied by more or less catarrh of its mucous membrane. The temperature is generally moderately raised. The amount of malaise varies greatly, but is often only slight.

The impossibility of recognising the disease during this early

stage is unfortunate, as, owing to its extreme infectiousness, it is the time at which much mischief in spreading the disease occurs. If a cold seems to be particularly severe as compared to the physical signs present, if the bouts of coughing have any tendency to be more frequent by night than by day, and particularly if they are accompanied by any tendency to vomiting, suspicion as to the case being one of whooping-cough should always be roused, and if any cases of the disease are known to be in the neighbourhood, these suspicions would be very much strengthened. Towards the end of this stage, the attacks of coughing will gradually get more severe, increasing in frequency, especially at night, and tending to become distinctly paroxysmal. With each attack the congestion of the face becomes more marked, and some of them are very likely to be accompanied by, or finish up with an attack of vomiting. At length all doubt is set at rest by one of the paroxysms ending with the peculiar whoop, when the second or paroxysmal stage has become established.

Paroxysmal stage.—This is the typical period of the disease, during which it is at its height, and when all its characteristics are most marked. The chief of these are the paroxysmal bouts of coughing. These may either come on apparently spontaneously or be obviously started by some external stimulus, such as a draught of cold air or the banging of a door, etc. The total number of attacks during the twenty-four hours varies within wide limits, from some 10 or 12 in slight cases up to 50 or 60 in severe ones. A certain grouping of the paroxysms is occasionally observable, one attack being rapidly followed by a second or even a third, which, however, are always less severe than the first of the series. The intervals between one paroxysm or group of paroxysms and the next are of more or less equal length, provided that no external stimulus, as mentioned above, should excite an attack. There is, however, a distinct tendency for the paroxysms to be more frequent and severe at night. It is a good plan to keep a record of the paroxysms, as a comparison of the numbers from day to day gives a fair indication of the general progress of the case.

When an attack is about to occur the patient frequently appears to have some sort of warning, and probably desists from whatever he may be doing—such as playing with his toys. He assumes an anxious look and may very likely get up and run to his mother or nurse, amongst the folds of whose dress he tries to bury his head. Then the spasm comes on. As a rule the child holds his head forward with the face looking a little downwards, with the mouth partly open and the tongue pushed forward as far as the lips, or even protruding

slightly beyond them. The spasm consists essentially in a series of expiratory explosions—during which all the usual appearances of asphyxia arise, and may persist until the onlooker begins to wonder if the child will not actually die from suffocation, as he assumes a horrible look with puffy eyelids, deeply congested face, with engorged veins and turgid neck. Then there is sudden relaxation with a long inspiration, during which the air rushing in through the larynx produces the whistling whoop or crowing sound, which may be repeated after a second or even a third spasm, and then, as the attack passes off, the child very frequently vomits the contents of the stomach. At the same time, or may be later, a pellet or even a tolerably large quantity of translucent, perhaps stringy, mucus is expectorated.

A period of quiescence now sets in, which varies very markedly in duration and intensity in different individuals and in accordance with the severity of the spasm; it may hardly exist. The child almost directly resumes his previous occupation, such as playing with his toys, apparently quite free from trouble and as though he had forgotten all about the attack. The play with which he occupies himself is nearly always, however, of some quiet kind. From this there are all stages, up to an extreme degree of collapse, the child falling back perfectly exhausted and apathetic, from which he may only be aroused by the onset of the next paroxysm.

Physical signs in the chest.—Where there are no severe complications the signs are very few. During the inspiratory stage of the spasm nothing can be heard in the chest with the stethoscope but the whoop, which is conducted to the surface. In the intervals a few rhonchi may be audible. Often, however, there is singularly little to be heard, and this is a point of some value in diagnosis—where a history is given of attacks of coughing which in severity are out of all proportion to the physical signs discoverable in the lungs and are especially frequent and troublesome at night.

In infants occasionally a slight *emphysema* occurs, which, with their soft-walled chests, may lift the sternum slightly forwards. This emphysema is probably due to over-inflation of the individual alveoli merely, without any breaking down of their walls, though this may occur, and indeed spread beyond the lungs and air passages into a more or less extensive "surgical emphysema."

The expression during an attack, as mentioned above, is very characteristic. *The tongue*, from its being pushed forward against the lower teeth, is likely to become abraded, and when only the two lower central incisors are present two small ulcers are frequently

formed on its under surface, one on each side of the frænum, which are exceedingly suggestive, though not absolutely pathognomonic of the disease. The tongue, as indeed the whole face, is often a little swollen.

The entire alimentary canal is probably congested or even inflamed, as not only does the vomit frequently contain a good deal of mucus, but there is often also a decided looseness of the bowels, which, however, only very rarely becomes at all serious.

Complications.—The most important complications, owing to their frequency, are those connected with the lungs, and it is noteworthy that the whoop is liable to disappear in those which are accompanied by fever.

Bronchitis.—There is almost always some catarrhal inflammation of the bronchial tubes present, which may, however, be so slight that the only evidence of it is that an occasional rhonchus may be heard. Generally, however, the bronchitis is well marked, the larger and medium tubes especially being affected—giving rise to well-marked sonoro-sibilant rhonchi; but occasionally it extends into the smallest tubes, when the grave signs and symptoms of acute capillary bronchitis are present, and this condition is nearly always accompanied with a greater or less extent of pulmonary collapse.

Broncho-pneumonia.—In addition to the bronchitis, patchy pneumonic consolidation not unfrequently occurs, and is of very great importance, as the high mortality of whooping-cough is very largely due to this complication; hence its onset is always serious, and if the child be constitutionally weak, and particularly if he be the subject of rickets, the outlook becomes extremely grave. The condition is recognised by the physical signs in the chest and remittent pyrexia and dyspnœa.

Lobar pneumonia with occasional pleurisy.—Lobar pneumonia occasionally occurs, but is very much less frequent than the other form. Pleurisy with or without effusion may accompany either form of pneumonia.

Acute bronchiectasis.—A rare condition recently described by Dr. Sharkey (St. Thomas's Hospital Reports, vol. xxii.) appears occasionally to start during an attack of whooping-cough. The physical signs and symptoms are so obscure that it has not yet been recognised during life as distinct from bronchitis.

Hæmorrhages.—Subconjunctival ecchymoses or slight attacks of epistaxis are common, but not in any way serious; on the other hand, should the hæmorrhage occur from a vessel in connection with the brain or spinal cord an extensive paralysis may be the result.

Acute nephritis has very rarely been met with after pertussis.

Nervous disturbances.—Various other nervous phenomena may occur which cannot be attributed to hæmorrhage.

There can be no doubt that the nervous system is profoundly disturbed. The very paroxysm of whooping-cough is like a nerve storm which originates in the pneumogastric centres of the medulla oblongata.

Epilepsy and insanity have been reported as having become apparent for the first time during an attack of whooping-cough or shortly afterwards, and localised paralyses, which from their mode of onset have been attributed to neuritis, have also been seen. Convulsions frequently occur, particularly at the termination of a severe paroxysm. They should always be carefully noted, as, although they may be merely the result of venous congestion produced by the paroxysm, and have no significance beyond being an evidence of the unsettled condition of the nervous tissue, they may be the prelude of some grave complication. They are also serious on their own account, as there is some evidence to show that death may be directly produced by them.

Defervescence.—The acuteness of the paroxysmal period gradually subsides. After about a month to six weeks from the onset of the disease the paroxysms become less frequent, and the whoop less definite and characteristic, so that in six weeks from when it was first heard it has generally subsided. If it should continue longer this is generally due either to habit or to the presence of adenoids in the pharynx. Occasionally, a week or two after the paroxysmal stage has begun to subside, there is a recrudescence, apparently due to the "catching" of a fresh cold, but unless this passes on to an attack of something more serious, it soon subsides and merges into the next stage, that of convalescence.

Convalescence.—This period may be rapid, particularly in the warm months of the year, but it may be very protracted, the child remaining listless and below par for a long time. It is during this stage that any latent weakness or tendency is so liable to manifest itself. The lungs are often long in clearing up, traces of bronchitis remain, and this condition may become chronic. However, fortunately, convalescence, though so often tedious, is usually complete, and the patient recovers perfectly.

Sequelæ.—Sequelæ, in contradistinction to complications, are not numerous. Any latent weakness, such as quiescent tubercle, is very likely to break out into renewed activity, and the occasional appearance of epilepsy, etc., has already been referred to.

Morbid anatomy.—After death, the changes that are found in the tissues are those of the various complications which have been already alluded to; there are none which can be considered as distinctive of the disease.

Diagnosis.—In the early stages it may be, and often is, impossible to make a diagnosis. There is usually but little difficulty when once the whoop has been heard.

Infants by no means always develop the whoop; but in their case a clue is often obtained from the fact that other members of the family have whooping-cough. In the absence of any such help the diagnosis is frequently extremely difficult. The paroxysmal character of the cough, accompanied by marked congestion of the face, vomiting, and possibly some nervous phenomena, are then the signs and symptoms on which the diagnosis is made; but the whole course of the disease may be run through without its true nature ever being suspected. The crow of laryngismus stridulus somewhat resembles the whoop of this disease, but the other characters of that condition are so well marked that there is but little practical difficulty in distinguishing between them. Some children have occasionally a whistling inspiration when they cough; this may cause some trouble at first, but a consideration of the other characters of the cough is generally sufficient to prevent a mistake.

There is a real difficulty in separating whooping-cough from certain cases with enlarged bronchial glands in the posterior mediastinum. In these cases the cough is paroxysmal, and accompanied by a regular whoop. It is only after some time has elapsed, and repeated examinations made, with a most careful weighing of all the evidence, that a correct conclusion can be arrived at.

Prognosis.—The prognosis of the uncomplicated cases is favourable; nevertheless the mortality is high, and is affected by one or more of the following factors: In early infancy the disease is always attended with anxiety, owing to the liability of extensive pulmonary collapse supervening, and this danger will persist beyond the first year of life if the subject be rickety, the softened ribs, the malnutrition and disturbance of the nervous system, all contributing to undermine the patient's chances of recovery. Lung affections, at all ages, are the most serious consideration, and in the large majority of cases the prognosis hinges on their severity. The condition of the nervous system is also an important factor. Very emotional children, and those who come of a highly neurotic stock, make bad subjects, and frequently have the disease in an aggravated form. Should a hæmorrhage occur, the prognosis is determined by its seat and

extent; but the general testimony of observers is one rather of astonishment that nerve lesions, which at first seemed so serious, are so frequently completely recovered from. Adenoids are justly credited with prolonging the convalescence.

Treatment.—Ordinary hygienic rules must be carefully followed. As soon as the condition is suspected or recognised, the child should be isolated from any that have not yet had it. He should be kept in two rooms—one for the day and the other for the night; and the atmosphere of the one in which he is should be maintained at an equable temperature of 65° Fahr. The importance of the two rooms is, that when the one is occupied the other may be thoroughly well ventilated by having the windows left wide open, care, of course, being taken that it is of the proper temperature before he returns to it. If at the onset any fever be present, it may be advisable to keep him entirely confined to bed until this subsides; but then, unless complications have set in, it is better for him to be up. It is of advantage to charge the air of the room with some vapour—by volatilising Friar's balsam, carbolic acid, creasote, naphthalene, turpentine, or eucalyptus oil. The suggestion for this came from the old-fashioned remedy of stirring Stockholm tar with a hot poker, or of taking children into the purifying chambers at gasworks. If the weather be favourable, the child may go out; but exposure to any inclemency of the weather must be carefully guarded against, and if any acute complication be present he must be kept within doors, where he should be allowed to amuse himself quietly, but be kept as far as possible from any form of excitement or emotional disturbance.

Feeding and diet.—So long as the vomiting is not troublesome, no precautions need be taken beyond ensuring that the food be light and wholesome. Meals should be frequent and small in quantity, and consist of beef-tea, gravy, milk, eggs, fish, bread, sponge-cakes, custards, stewed and fresh fruit. If the vomiting becomes at all serious, it is a good plan to give some food as soon after the paroxysm as possible.

The list of *drugs* that have been brought forward at one time or another, as specifics for this disease, is a long one, yet none have been proved to be worthy of the title; still, some are found occasionally to be of decided use.

In uncomplicated cases belladonna, in combination with bromide of potassium, has been a general favourite; a very suitable prescription for a child about two or three years of age being—

℞

Extracti belladonnæ liquidi . . .	♏ ¼
Potassii bromidi	gr. iii
Glycerini	♏ x
Aquam destillatam	ad ℥ ii

Misce. Fiat haustus.

To be taken every four hours.

The belladonna should be pushed until slight flushing occurs, but not so far as to cause dryness of the mouth or stomach irritation. Trousseau recommended that the belladonna, or preferably atropine, should be gradually increased over a period of three days, until the pupils began to dilate, and then in just sufficient quantity to maintain this condition for about a week.

Antipyrin or phenacetin have given good results in one, two, or three grain doses, every four or six hours.

Carbolic acid is useful, and well borne even by infants, the *glycerinum acidi carbolici* being a good preparation to use in doses of four or five minims.

If there be much insomnia, or any tendency to convulsions, butyl chloral hydrate, given in grain doses every hour, is often most efficient. In very severe cases, where the number of spasms exceed twenty in the day, Dr. Henoch has pushed morphine in doses varying from $\frac{1}{12}$ to $\frac{1}{4}$ grain, with the best results. Bromoform, in minim doses, has considerable effect in controlling the vomiting, and appears frequently to distinctly reduce the severity of the paroxysm.

Expectorants are useful, especially if there is any considerable degree of bronchitis present, ipecacuanha or squills being generally used. They can, of course, be combined with almost any of the foregoing drugs.

Local treatment.—Local treatment, by direct application either by brush or spray, has been very strongly advocated. The latter is probably preferable, as the use of a brush is liable to terrify the child, and emotional disturbances should be avoided. However, excellent results have been recorded from the frequent painting of the larynx and adjacent parts with a two per cent solution of resorcin, and quite recently very weak solutions of formalin have been recommended to be tried in a similar way.

The external application of turpentine, or ammoniated camphor liniment, or other stimulant to the chest wall has many advocates.

F. G. Penrose.

DENGUE

Syn. Dandy Fever, Break Bone Fever

A specific infectious malady occurring in rapidly spreading epidemics, and attended by the sudden onset of severe pains in the limbs and joints, a high temperature, and a marked eruption of a rubeolar character.

Geographical distribution.—So far as is known, dengue may occur anywhere in tropical or sub-tropical countries. In Europe it has appeared in the Turkish, Grecian, and Russian (Black Sea) ports; in America it affects chiefly the West Indies, but has been known to extend northwards as far as Philadelphia, and southward to the Argentine. All countries bordering on the Indian Ocean have been frequently visited by dengue, and the Far East and Australia have suffered from epidemics of the disease. It especially tends to spread along the sea coasts, and inland along the banks of rivers, thus resembling yellow fever, and rarely invades elevated districts.

Dengue attacks all and sundry, from young children to persons of extreme age. When it breaks out in a village, in a school, or barracks, the majority of persons of the community are quickly seized. The disease tends to follow the lines of human intercourse; a ship bearing infected passengers frequently setting up fresh foci of infection at each port of call. Hot weather favours its development, and as a general rule cold weather stays its progress. Like other maladies of this class it exhibits recurrent periods of greater intensity and wider distribution.

Nothing is known concerning the bacteriology of the disease.

Incubation.—One to five days is the period of incubation usually assigned to dengue. During incubation symptoms seldom show themselves, but in some instances muscular aches and joint pains precede the onset of fever.

Symptoms.—Dengue usually attacks quite suddenly; in the majority of instances it is ushered in by headache, pains in the back, limbs and joints, fever, chilliness, or even a rigor and an intense feeling of weakness. Or the initial feeling of prostration may continue for a few days, accompanied by giddiness, nausea, alternate sensations of chilliness and heating, flushings, and a

gradual development of rheumatic pains in the limbs, body, and joints. The joint pain is peculiar; the first symptom may be a sudden seizure of pain in one finger, or the pain may rapidly extend to almost every joint in the body; or it may fly from one joint to another, disappearing as suddenly as it came.

The first eruption.—On the third day the temperature rises, it may be, to 102° F., or even to 106° F.; the pulse becomes rapid; the skin hot and dry; the face looks swollen, and the whole body is covered by a rash resembling that of scarlet fever; the tongue, moreover, presents an appearance similar in many respects to the "strawberry" tongue of scarlet fever, and the throat shows a somewhat similar congestion.

The remission.—In from twenty-four to forty-eight hours the first eruption disappears, all feverish symptoms subside, and for a period of from two to four days the patient feels fairly comfortable.

The second, or terminal rubeolar eruption.—A return of fever, it may be of slight amount and duration, is attended by a recrudescence of joint-aches and an eruption of circular, somewhat elevated, discrete, reddish spots on the hands, wrists, and forearms; and in a few hours the neck and face, the trunk, and finally the lower extremities are similarly covered. A coalescence of spots may give the eruption an urticarial appearance, or even cause a general diffuse redness of the skin. In a day or two, attended by a profuse sweating, epistaxis, or an intestinal flux, the temperature falls to the normal, and then below it. Desquamation of a furfuraceous character succeeds, and for some twenty days the patient continues to shed the epidermis in fine, dusty particles.

Sequelæ.—The symptoms, after the temperature falls, gradually fade away into rheumatoid pains, at times, however, of a distressing character, attended by swollen and painful joints. Both large and small joints are attacked, and, as the muscles are involved in the affection, considerable stiffness, and it may be inability to move freely induce wasting of the limbs from non-use. Convalescence is often tedious, except in the case of children, and it may be interrupted by relapses which continue the disease for several months.

More remote sequelæ are—adenitis, more particularly of the cervical glands; orchitis; albuminous urine; hæmorrhage from nose, mouth, bowels, or uterus; and such cutaneous ailments as boils, pruritus, and evanescent eruptions.

Variety in type.—Dengue in some cases is so mild in type that it causes the patient but little inconvenience. A slight sore throat with some pains in the limbs and back, and a feeling of

lassitude may be the extent of the symptoms. Instead of the favourable course, however, dengue may assume a serious form; the skin and features become cyanotic, collapse supervenes, and the patient dies in a comatose state. This form constitutes the "black fever" of Calcutta natives. Variations occur in the appearance of the rash, which at times is scarcely perceptible, or the primary rash may be rubeolar in character. Children, when the temperature runs high, frequently develop delirium, and alarming convulsions sometimes usher in the disease.

Diagnosis.—In tropical countries the initial symptoms are apt to be confounded with a malarial fever. As the disease advances influenza suggests itself; but the appearance of the rash raises the question of scarlet fever or measles. Influenza is frequently confounded with dengue, and the outbreak of the modern epidemic of influenza in 1888, in Hong-Kong, was at first regarded as being one of dengue, the more so as in many cases a marked rash was occasionally present. Scarlet fever does not appear in epidemic form in tropical countries. Measles occur in the tropics, but it seldom attacks adults, and is slow in its progress and spread compared with dengue.

Prognosis.—An attack of dengue of average severity justifies a favourable prognosis, although several of the complications and sequelæ in the young or old may lead to a serious or a fatal issue. The "black fever" of Calcutta already referred to shows, however, how severe dengue may become. One attack of dengue confers some degree of immunity against a recurrence.

Treatment.—In all respects dengue is to be treated as other specific eruptive fevers, such as scarlet fever or measles. The patient is to be confined to bed, and placed on the usual febrile regimen as to diet. Constipation may be relieved by saline aperients. Joint and muscular pains may be so severe as to require the external application of anodyne liniments, and the administration of morphia either by the mouth or subcutaneously; the tincture of belladonna, in 15 minim doses, repeated thrice at intervals of one hour, has attained a reputation as a means of allaying the suffering peculiar to dengue. Cold or tepid sponging affords considerable relief if the temperature be high.

Convalescence may be usually considered to commence after the tenth day, when a general tonic treatment is required.

Isolation of the sick and removal of exposed persons to a non-infected house or district affords but small protection when dengue is epidemic.

James Cantlie.

BERI-BERI

A specific peripheral polyneuritis, characterised by disorders of sensation, paresis, changes in the electrical response of the muscles and nerves, and widespread vasomotor disturbances of such a nature as to cause either a general anasarca or an atrophic appearance of the body. The disease is one of environment, and may become endemic in localities or abodes. It is usually attended by a high mortality, death resulting from exhaustion, paralysis of the heart, or of the muscles concerned in respiration.

Geographical distribution.—Originally described by Bontius in India, the disease has in recent years been scientifically studied in many tropical, sub-tropical, and even temperate climates, more especially in Japan, in Brazil, and in the Dutch East Indies. In addition to its occurrence in these several countries beri-beri is met with in the southern provinces of China, in Annam, throughout Malaya, Borneo, Fiji, New Caledonia, and even amongst natives of, and the Chinese immigrants in, Australia. In America it is found amongst the fishermen of the North Atlantic sea-board, in Havana, at Panama, in Brazil, and in the Sandwich Islands. In Africa cases have been met with from the neighbourhood of Lake Nyassa and the Congo (Manson). Lastly, attention has been drawn to the disease in several places in Europe, more especially in Ireland, where, in the Richmond Asylum, Dublin, during 1896, 1897, and 1898, a marked outbreak of the disease has been described by Dr. Conolly Norman.

Etiology.—The cause of beri-beri has not yet been ascertained. A bacterium was figured and described by Pekelharing and Winkler as the result of their investigations in Java and Sumatra, but the specific nature of the organism has not been confirmed by subsequent observers.

A diet deficient in nitrogen, such as rice, especially when the grain is of inferior quality and deprived of its outer covering, is by many competent observers held to be associated with outbreaks of beri-beri. The chief reason for this belief is that a change to a more nitrogenous diet is frequently followed by the disappearance of the disease. In the Japanese navy, where beri-beri (kakké) was very frequent, a change in diet of the kind indicated was followed by highly satisfactory results. There are several arguments against

rice being a direct factor in the etiology, none being more potent than the late peculiarly isolated outbreak in the lunatic asylum in Dublin. By some the disease has been ascribed to the consumption of certain species of fish imperfectly cooked.

Of other assigned causes there are many. Overcrowding, malaria, climate, anæmia, may furnish a favourable nidus for an outbreak of beri-beri by lowering the vitality and diminishing the bodily powers of resistance, but they cannot determine the onset of a disease of so specific a character. Beri-beri is essentially the disease of environment or habitation. It would seem as though a dwelling or ship became infected, and that the disease clung to the place. As a consequence healthy persons taking up their residence in quarters vacated by beri-beri patients readily become infected.

The evidence goes to show that beri-beri is dependent upon a toxic influence, probably parasitic in nature, having its habitat, in all probability, outside the human body. The disease is not regarded as directly contagious, nor is the beri-beric considered to be personally infectious. The writer, however, found what appeared to be direct communicability take place in a hospital for Chinese in Hong-Kong. A number of cases of beri-beri had been admitted to a general ward, and after a time beri-beri developed in several patients suffering from open sores in the same ward, whilst it passed over those who showed no wounds. Young men are most frequently the subjects of beri-beri, but with the exception of infants and octogenarians it has been known to attack persons of any age and of either sex. The rich as well as the poor suffer, but the disease is propagated and thrives in the overcrowded, insanitary native hovels, in the barracks where native soldiers congregate, in the ill-constructed, insanitary, and crowded temporary dwellings on newly-opened plantations. Beri-beri is also most frequently met with at low levels, and more especially, but by no means exclusively, along the sea-coast.

The Dutch observers in Sumatra established the fact that between the period of exposure and the development of clinical signs and symptoms of the disease, or, in other words, during **the incubation period**, careful investigation will show that there exist several latent signs. Of these the chief are a slight œdema along the crests of the tibiæ, and important variations in the response of the muscles and nerves to electrical stimuli. The minimum period of incubation of beri-beri is about five weeks. The maximum period may extend over several months.

Symptoms.—The "invasion" period of beri-beri—the "initial

phase "—presents the following signs and symptoms :—slight œdema along the tibial crests; pale and swollen-looking features; a slight rise in temperature, which may be very evanescent, lasting only a few hours, but nevertheless none the less constant; palpitation; a small, irritable pulse; some apparent increase of cardiac dulness; violent cardiac impulse; a prolonged first and reduplicated second sound; shortness of breath on exertion; difficulty in walking quickly and going up and down stairs owing to muscular stammering; circumscribed anæsthesia and pain on pinching the muscles of the lower extremities.

When beri-beri has developed there will always be found in the calf of the legs a patch which is insensible to a light touch, and to both galvanic and faradic currents. The leg muscles, and afterwards the muscles of the thigh, become painful when pinched, and the anæsthetic areas increase in extent. The muscles become weaker, their quantitative irritability is diminished, and very slight resistance is sufficient to stop extension of the leg and flexion of the thigh. The muscles of the calf, when contracted, bulge abnormally, but although painful to pressure there is seldom found any idio-muscular contraction, nor are they usually irritable to percussion. When the patient attempts to rise from his bed, or to lie down, considerable awkwardness is noticeable, and when he attempts to walk the gait is markedly abnormal. He wavers when he tries to stand with his eyes closed, nor can he stand on tip-toe, nor on one foot. During walking the patient raises the foot from the floor with difficulty, the toes leaving the floor last, and, after lifting the foot high and pushing it forwards, suddenly drops it on the floor. The dynamometer also shows that the muscular power of the hands and arms is distinctly lessened. As the disease progresses the anæsthetic areas in the legs may extend from the knee along the inside of the limbs to the heel; and the thenar and hypothenar eminences in the hands become anæsthetic, whilst as yet the parts of the hand beyond are unaffected. The muscular sense is undisturbed, the patient localises well and can imitate with one limb passive movements made for him with the other. The condition of the reflexes is characteristic. The knee jerk completely disappears, either from the onset of the initial phase or after a few days. Ankle clonus is absent, but the superficial abdominal and scrotal reflexes are readily elicited. The muscles, more especially those supplied by the external popliteal nerve, exhibit the reaction of partial degeneration. Irritability to the faradic current is suppressed, whether the current is applied directly or indirectly, and

there is also diminution of direct and indirect irritability to the galvanic current. The subsequent symptoms depend largely on the seat of the nerves attacked.

The dilated heart may give out, or this condition, combined with a sudden effusion into the pericardium, may cause cyanosis, dyspnœa, or syncope. The respiratory muscles, on the other hand, may become paralysed, causing sudden death by asphyxia. Vomiting is a grave sign, and death, when it occurs, is usually sudden. In favourable cases the œdema, if it exists, disappears, the paralytic signs are first stayed in their advance and then abate in their intensity. Power returns to the hands and legs, the irritability of the heart lessens, dyspnœa disappears, and after three months or so the patient is usually able to get about, or even follow his employment. Occasionally it happens that paresis remains for an indefinite period. During the development of these paralytic signs and symptoms the general health of the patient is wonderfully good. The digestive organs present nothing amiss, and the urine seldom betrays any signs of renal disturbance.

Varieties.—The three most pronounced types of beri-beri are the œdematous, wet, moist, dropsical; the atrophic, dry; and the mixed. In addition to these names, however, we are familiar with such terms as "acute" and "chronic" beri-beri, "foudroyante," etc. It is doubtful whether any one of these is worthy of the name of a variety, as it is possible the one is but the precursor or sequel of another, a mere predominant symptom being seized upon to constitute the basis of differentiation.

1. The *œdematous, dropsical, "wet" or "moist"* form of beri-beri is characterised by a fairly general œdema. The anasarca closely resembles that met with in a case of acute Bright's disease, but the urine, although presenting occasionally a slight albuminous cloud on boiling, shows none of the characteristic features consequent on acute nephritis. The œdema is at times partial, often missing the scrotum, and at times changing its site. The serous cavities may be the seat of a large amount of effusion, the pericardial cavity being especially liable to effusion; but the pleural cavities may be filled to such an extent that breathing is greatly hampered and the lung space so diminished that asphyxia supervenes.

2. The *atrophic, "dry," or purely paraplegic* variety of beri-beri is, as the names imply, associated with shrinking of the tissues of the body. The muscles are flabby and the fat of the body disappears. The patient, as regards his alimentary and renal condition, may

be pronounced healthy, and it is to a paralysis of the laryngeal or respiratory muscles that he usually succumbs.

3. *Atrophic and œdematous*—"*mixed*"—*beri-beri.*—When atrophic symptoms are obscured by serous effusion into the muscular and the connective tissues, and when, also, the serous cavities are the seat of a similar effusion, the clinician, pledged to the cognisance of a "wet" and a "dry" variety of beri-beri, will find great difficulty in referring the disease to its particular variety. Hence the adoption of the term "mixed," in which the signs and symptoms of the "wet" and "dry" varieties are combined.

In all these divergencies, however, one symptom remains constant, viz. the electrical modifications of the nerves and muscles. It would be well to dispense with these distinctions, except in so far as they indicate stages in the disease, because œdema is only a secondary phenomenon, and if the mixed form is taken as the type, the dropsical and dry forms are but a quantitative modification of it.

The motor disorders.—The most constantly paralysed muscles are the groups supplied by the external popliteal nerves, viz. the peronei, and the extensors of the toes; the next most frequently affected muscles are the flexors of the toes. The extensors of the knee and the gluteal muscles are also liable to be involved in the paresis, whilst the adductors and the knee flexors escape. In the upper extremities the extensors of the hand and fingers, the supinator longus, the triceps, the flexors of the hand and fingers are, in the order given, the muscles liable to attack. In addition to these the abdominal muscles, the diaphragm, and the intercostal muscles suffer. Even the muscles supplied by the cranial nerves may become involved; the muscles of expression and the muscles of the eyeball having been known to become paralysed. The laryngeal muscles are also frequently involved, with the result that sudden death ensues from asphyxia.

Disorders of sensory nerves.—The sense of touch is first lost on the inner aspect of the calf of the leg, then on the dorsum of the foot, and finally sensation may be lost everywhere below the knee. In the upper extremities sensation disappears first on the anterior aspect of the wrist, then over the thenar and hypothenar eminences, and finally over other parts of the hand; the ends of the fingers being the last places from which it vanishes. Anæsthesia may overtake the whole of the upper limb as far as the shoulders. Anæsthetic areas may also be met with over the anterior aspect of the trunk, reaching as low as the umbilicus.

Heart affections.—The heart is early affected in beri-beri. Not only are there marked subjective symptoms, but there is a pronounced enlargement of the cardiac area, especially towards the right, and pathological evidence shows that there is hypertrophy accompanied by dilatation of the right ventricle. The state of the ventricle explains the dropsical effusion into the tissues and the serous cavities and the other effects of venous obstruction.

Post-mortem appearances.—According to the type of beri-beri which has proved fatal, so do the post-mortem evidences vary. In the "wet" variety serous effusions may be found in the subcutaneous and intermuscular tissues and in the serous cavities of the body; in the "dry" variety, on the other hand, the muscles when cut into reveal the yellowish-brown colour characteristic of atrophy. It must be remembered, however, that œdema to some extent has always existed at some period of the disease, and pericardial effusion in particular is one of the most constant features of beri-beri. It is in the heart itself, however, that pathological change is to be sought for. Hypertrophy of the right ventricle is always present, accompanied by a dilatation varying from, it may be a small, to an enormous extent. The heart muscle is often pale, but microscopic examination shows that this is not usually due to fatty degeneration. Of the other organs the lungs may be œdematous, the liver congested, the spleen increased in bulk and weight, and the blood in the large veins in a fluid state. The examination of the nervous system shows that, in the nerves generally, a state of peripheral neuritis and nerve degeneration exists, and that the lesion diminishes in intensity as the centre is approached. The anterior roots of the spinal nerves show no pathological change, but in the posterior roots, more especially in the part between the ganglion and the nerve trunk, atrophied fibres are met with. In the central nervous system the most constant change is an alteration (it may be an atrophy) in the large cells occupying the anterior cornua of the spinal cord.

Prognosis.—During an attack of beri-beri it is well-nigh impossible to venture on a prognosis; for cases of seeming mildness prove fatal, whilst cases of apparently a severe type recover. In general about 20 per cent of those attacked die; but the numbers vary, it may be as much as 10 or even 15 per cent either way. Unfavourable signs are: cardiac and vascular changes, such as a quick and feeble pulse, epigastric pulsation, throbbing of the blood vessels in the neck and increase in the cardiac area; extensive serous effusions into the peritoneal, pleural or pericardial cavities; failure

in power of the respiratory muscles; marked diminution in the quantity of urine passed; and vomiting. The last-mentioned feature supervening, as it sometimes does during the course of an acute attack of beri-beri, is a very unfavourable sign.

Diagnosis.—Beri-beri has to be diagnosed from peripheral neuritis, due to alcohol or to malaria, from locomotor ataxy, and from epidemic dropsy. In epidemic forms of the disease the diagnosis is readily enough arrived at, but when sporadic cases, or when even limited outbreaks occur in what are regarded as non-beri-beric countries, as in Ireland, the recognition of the disease is attended by obvious difficulties. Reliance must be placed upon the presence of œdema, limited, it may be, to the front of the shins; upon the absence of knee jerk; upon the tumbling action of the heart; pain on pinching the limb muscles and patches of anæsthesia on the legs and perhaps the arms. If electrical testing is available the diagnosis is greatly facilitated.

Treatment—*Prophylaxis.*—Seeing that beri-beri is a disease of environment it is necessary to correct or alter the immediate surroundings of those exposed to the disease. Disinfecting the abode, the furniture, and the clothing of beri-berics serves to check the numbers of those attacked; but it is only by evacuating the premises, and it may be leaving the locality where beri-beri is endemic, that an outbreak, say, amongst troops in barracks, coolies in coolie quarters, and prisoners in a jail, may be stamped out. In the case of the individual it is only by removal to an untainted locality that a cure can be confidently hoped for.

Rest in bed ought to be insisted upon and sudden movement or exertion forbidden. The diet must be liberal in the item of nitrogenous elements, and if rice has been the staple food heretofore it should be supplanted by bread, meat, milk, and fresh vegetables. When it is impossible to immediately quit the abode, as on board ship, those afflicted with beri-beri should be granted the best sleeping accommodation possible, and during the day should be brought out into the open air.

The state of the heart and of the circulatory organs generally calls for medicinal treatment. Cardiac stimulants, such as digitalis, may be administered with good effect; nitroglycerine in the form of the liquor trinitrini (1 min.), or tabellæ nitroglycerini B.P. (1 tablet) should be at hand for emergencies of cardiac failure. Amyl nitrite may be inhaled from a crushed capsule with the same intention. The functional condition of the heart in beri-beri is so little understood that it is difficult to justify, far less to explain the beneficial

action of these drugs, except it be that by the administration temporary relief is afforded to the enlarged right ventricle, by diminishing the resistance of the blood vessels to the onward passage of the blood.

Aspiration of first one, and (if necessary) later the other pleural cavity affords relief in dyspnœa, and the writer found benefit by venesection in one case of threatened asphyxia and by aspiration of the pericardial effusion in another.

When the patient is convalescing strychnine is the best medicinal tonic; but massage, electrical stimulation and general tonic treatment favours recovery. It was at one time believed that beri-beri always relapsed, and that in about twelve months a recrudescence was to be looked for. No doubt this is the case when the patient returns to an infected environment, but by residence in a healthy locality such a relapse may be almost certainly avoided.

JAMES CANTLIE.

EPIDEMIC DROPSY

An epidemic disease of variable mortality and lasting from three to six weeks; characterised by œdema of the lower extremities or of the entire body, accompanied by pyrexia, by gastric and intestinal irritation, by aching in the limbs and trunk, and frequently by a cutaneous rash of a rubeolar appearance.

Geographical distribution.—Since Dr. Kenneth M'Leod first described the disease in Calcutta in 1877, several observers have recorded outbreaks of the disease. In Assam, in Lower Bengal, and in Mauritius, well-defined occurrences have taken place, and, in all probability, outbreaks of this particular malady have developed at several places on the littoral of the Indian Ocean.

Etiology.—Epidemic dropsy appears to be communicable from one member of the community to another, and is mainly confined to the adults of both sexes of a family. It occurred in Calcutta during the cold weather, disappeared completely during the hot season, and for three successive winters, 1887 to 1890, recurred persistently; since then the disease does not seem to have re-appeared. No European is known to have contracted the disease.

No bacteriological investigations have been as yet communicated concerning the causation of epidemic dropsy.

Symptoms.—Initial symptoms vary. In some instances the disease is ushered in by the dropsical effusion; in others, fever first attracts attention; or again general malaise or intestinal flux precede all other manifestations.

The œdema appears in the feet and ankles and may extend beyond the lower extremities to the whole body, sometimes lasting for a considerable period. Pleural and pericardial effusions have sometimes been noticed. Fever may usher in the symptoms, may accompany the dropsy or appear only during its subsidence. It is seldom the thermometer registers higher than 102°. Vomiting is seldom distressing; diarrhœa or even dysentery of a mild type occasionally occurs. In addition to itching and burning of the skin, a general exanthematous rash, of a rubeolar character, is a common, but by no means a constant, accompaniment. The general signs and symptoms include a weakened pulse, breathlessness, and marked anæmia and prostration. Nocturnal pains in the limbs have been frequently observed.

Occasional signs and symptoms of pneumonia, œdema of the lungs, cardiac dilatation, scurvy, and albuminous urine have all been recorded as complications of the disease.

Diagnosis.—The only disease likely to be confused with epidemic dropsy is beri-beri. In fact many observers positively assert their identity; whilst on the other hand it is possible, nay probable, that many cases at present classed as beri-beri will prove to be of the nature of epidemic dropsy. The one characteristic feature of beri-beri which serves definitely to stamp its specific nature is the nervous and paralytic affections, and these are absent in epidemic dropsy. Moreover, beri-beri is more chronic and never complicated by a cutaneous eruption, nor is fever a prominent feature.

Mortality.—In the Calcutta epidemics a death-rate of from twenty to forty per cent of those attacked occurred. On the other hand, in the Assam outbreak, no fatal cases were known.

Treatment.—Such remedial treatment as a weakened circulation demands, and as is appropriate in urgent cases of dyspnœa or apnœa is called for in the treatment of epidemic dropsy.

Southey's trocars are indicated as a means of relieving the dropsical effusion, and even aspiration of the pleura or pericardium may be necessary. During convalescence anæmia is the most prominent condition which requires treatment.

JAMES CANTLIE,

ORIENTAL SORE

Syn. Delhi Boil; Bagdad Sore; Biskra Button; Aleppo Evil

A specific inflammatory affection of the deeper layers of the skin, which, commencing as a papule, soon crusts over, and spreading by phagedæna, develops an ulcer of an indolent character. The healing is protracted, and a permanent scar, a "date" mark, remains to indicate the seat of the affection.

Geographical distribution.—The various synonyms indicate the principal places in which this peculiar affection is met with. In Europe, Greece and Crete seem to be the only countries in which the disease has been noted. In Africa it occurs in Morocco, Egypt, and certain parts of the Sahara. In Asia: Bagdad in Mesopotamia, Aleppo in Syria, Delhi and Mooltan in India, are the chief seats of the disease. But Arabia, Persia, and Turkestan are known also to harbour the malady. Some ten years ago persons residing in the town of Bahia, Brazil, were declared to be affected with true "Oriental Sore."

What the specific infective matter may be is unknown. Objects that appear to be minute parasites in the "boil" have been described by Dr. Smith as the ova of Distoma, by Dr. V. Carter as the spheroids and mycelium of a special parasite, and by Dr. Cunningham as zoocysts or sporocysts which are also met with in the water in some of the districts where Oriental sore is endemic. Biting insects are in all probability the carriers of the infectious matter, as it is the exposed parts of the body that are almost solely attacked.

Etiology.—It would seem as though a special state of climate and constitution were necessary for the development of the disease, as it occurs in countries possessing for the most part a dry, even arid, climate, and it appears towards the end of the hot season, when the vigour of those attacked is probably at its lowest. Insanitary surroundings favour the development of Oriental sore. All nationalities, both sexes and all ages, are liable to attack, and the disease seems to occur in special prevalence, not only at certain seasons, but also during certain years.

One attack as a rule confers a permanent immunity.

Communicability.—The disease is not confined to human beings. Dogs and horses are stated by Fayrer to suffer from a

disease in India closely resembling Oriental sore. Both man and the lower animals can be inoculated by discharge from the surface of ulcers. Attempts at inoculations from cultures of certain micrococci obtained from the centre of the papules have hitherto failed.

Symptoms.—On some exposed part, or parts, of the body, usually the face, neck, or extremities, the attention of the patient is drawn to a small itching papule, or to a number of similar pimples on different parts of the body. When looked at carefully the papule appears pink in colour; it is frequently situated around a hair follicle, and the epidermis over it is seen to be dry and loose. Gradually the subcutaneous tissues around become infiltrated and feel boggy to the touch; the intense itching alternates with occasional stinging pains; and a slight oozing from the surface and moistening of the skin causes the epidermal cells to cake, and finally to crust. Underneath the crust an ulcerating surface develops, at first quite superficially, but gradually the ulceration extends deeper and wider, presenting a rather sharply cut and indurated edge. The crusts fall and re-form from the thin ichorous material which exudes. Around the primary papule others form, and, as these coalesce, they add to the extent and intractability of the sore. An individual sore is usually about one inch in diameter, and there may be several on different parts of the body. It is believed also that any ordinary boil or wound may take on the characters peculiar to Oriental sore. After many weeks, or more likely months, the wound shows signs of healing. Slow in its development, however, the "sore" is still slower in its disappearance, and it leaves behind the peculiar "date" scar, indelibly impressed. The cheek and nose are favourite sites of the disease, and a large "date" mark on either of these may be followed by permanent unsightliness.

Prognosis.—There is but little danger to life from Oriental sore. Were the wound to be attacked by erysipelas, or become markedly phagedænic, alarming symptoms might ensue.

Treatment.—Destruction by caustics or cautery of the primary seat of infection has been frequently attempted, but the results are not encouraging; and in the absence of any known specific application, it is wiser to pursue an expectant treatment, viz. attending to the general health, seeing to the sanitation of the house and environment, applying soothing antiseptic remedies to the sore whilst it is indurated and irritable, and promoting healing by cleansing the wound and protecting its surface.

JAMES CANTLIE.

VERRUGA PERUANA

A specific, general, infective, inoculable disease, characterised by constitutional symptoms and a special granulomatous eruption. It seems to be quite distinct from framboesia.

The disease is peculiar to certain defiles penetrating the tropical Andean mountainous districts of the departments of Ancache and Lima, which are watered by rivers overflowing each January and June. There are no limitations as to age, sex, or race. Domestic animals, such as dogs, pigs, fowls, turkeys, horses, mules, llamas, cows, and asses contract the disease, which assumes remarkable proportions in the solipeds.

Eight to forty days are generally allowed to be the **incubation period**; some observers give even a longer range.

The **invasion** symptoms may be of very different degrees of severity. The malady may be so intensely virulent that the patient succumbs before the eruption appears. Usually there is an insidious onset with general malaise, which gradually becomes intensified. Pain and fever are prominent. Rheumatoid pains, with nocturnal exacerbations, shift from joint to joint, and are often terribly severe. Muscular pains, also, may produce rigidity and contractions. A great variety of febrile types are observed, of which the acute arthritic and low typhoid may be especially noted. The fever may be intermittent, and is generally hectic; the intensity corresponds with the virulence of the infection. A marked anæmia sets in, with profound prostration, and these states are apt to be increased by the subsequent ulceration and bleeding of the eruption. Hæmic murmurs may develop, serous effusions are frequent, and the spleen, and sometimes the liver, enlarges. The *eruption* appears after a period of twenty days, or only after six or eight months, or even one year, it is said, and when it evolves the general symptoms tend to abate. Its duration may be put at about two to eight months, but varies widely according to the number of outbursts, and the quantity and volume of the elements and attending complications. It appears usually in the skin of the extremities and face, and spreads thence to more or less of the rest of the body, and to the mucous membranes, and even the splanchnic organs and serous membrane. The distribution is, however, most variable. The eruptive elements may be small and superficial, or develop more deeply in the cutis

and subcutaneous tissue, and then attain the size of an orange, or more, and give rise to grave cachexia by their sloughing and bleeding. The smaller type begins as a tiny red spot, which develops into an itching, shining papule, and finally into a very vascular, red "wart" (whence the name *verruga*), which may become pedunculated. The eruptions gradually die away with exfoliation or bleeding, or ulceration and crusting. *Histologically* the granulomata are said to bear a striking resemblance to sarcomata, and to be specially characterised by a remarkable vascularity. According to Yzquierdo, they are caused by a specific bacillus, which is found between the cells, and also thrombosing the vessels.

The **diagnosis**, in the pre-eruptive stages from malaria, rheumatic and typhoid fevers, is often very difficult. Verruga is a very serious and dangerous affection.

There is no specific **treatment** known to be effective. The sufferer should be removed at once to as healthy a locality as possible at the sea level.

T. Colcott Fox.

FRAMBŒSIA

A highly contagious, but not hereditary, specific, general, chronic, infective disorder, characterised by a cutaneous granulomatous eruption of special aspect, resembling a raspberry, whence the name is derived through the French "framboise." It is endemic in some of the West Indian Islands ("yaws"), especially Dominica; in parts of Brazil and the Spanish South American colonies ("bubas") and Guiana; in Fiji ("koko"), Loyalty, New Caledonia, and other Melanesian Islands; in Ceylon ("paranghi"), along the Coromandel Coast, Assam, and the East Indies; in the Moluccas, the East Coast of Africa, along the Mozambique Channel, and on the West Coast about Sierra Leone. One attack renders the subject immune for the most part. It is not syphilis altered by race, climate, and locality, for both diseases breed true in the same community; syphilis can be inoculated and run a typical course in a yaws subject, and healthy children are born of women actually, or recently, suffering from yaws. Moreover, the incubation stages are different, and many of the secondary symptoms characteristic of syphilis, such as iritis, sore throat, and usually the adeno-

pathy, are absent. Tertiary symptoms do not follow, it is said, though ulceration is not unfrequent.

Inoculation occurs through any of the breaches of surface, so frequent in unclothed people living under unhygienic, crowded, miserable conditions.

After an **incubation period**, variously stated from two to ten weeks, or a somewhat shorter average time (twelve to twenty days) in experimental inoculations, an *initial papule* appears at the seat of inoculation in a considerable proportion of cases, though not invariably, and develops into a moist, yellow, fungating granuloma, similar to those of the generalised eruption, and sometimes persisting for a long period as the "mother-yaw." Simultaneously with the initial papule, or shortly after, but usually within ten days, a granulomatous, more or less generalised, eruption appears in successive crops, and may last as a whole from three months to four years, averaging about two years. The eruption evolves as itching papules, the size of pin-heads, which may abort in the early stages with the separation of corresponding scales. Some authors draw special attention to the occurrence of such furfuraceous desquamation in the earlier stages of the effection or at later periods. As a rule the enlarging papule bursts through the epidermis and discloses a central, yellowish, softened point which may simulate a pustule. Finally, an abruptly-raised, painless excrescence is formed like "proud flesh," or somewhat resembling mucous tubercles or condylomata, or, in certain rarer dry states, warts. These efflorescences may reach the size of a small pea, or even a walnut, and may form larger patches by confluence, or become annulate. They tend to be covered with a thin scab, and on disappearance after some weeks leave a stain lasting a few or many months. In many cases successive crops continue to appear. The eruption may be generalised and copious, or scanty and localised. The lips and nostrils may be implicated, but otherwise the mucous membranes appear to escape, as do the viscera. In the conditions under which framboesia occurs it is not surprising that secondary ulcerations should result in many cases. The causal micro-organism has not yet been definitely established.

Constitutional symptoms, such as fever, are absent, slight, or rarely severe, and, as a rule, the subjects continue their usual avocations.

Treatment.—Isolation is necessary to prevent the spread of the disease. In ordinary cases, where the general health is good, the disease runs its natural mild course under proper feeding and hygiene, and the prognosis is most favourable. Mercury and iodide

of potassium have been much used, and the reports as to their action are most conflicting. The local application twice daily of chromic acid, or a mixture of picric and carbolic acid to dry up the granulomata is recommended; and for some of the later and more persistent lesions nitrate of silver and sulphate of copper are useful.

T. Colcott Fox.

SYPHILIS

Syphilis is a specific contagious disease, communicable by direct inoculation. Its course is characterised by a primary lesion (chancre), by early constitutional (secondary) symptoms, and by late constitutional (tertiary) symptoms.

Frequently a final stage is to be observed, a post-syphilitic fibrosis, especially well marked in the blood vessels, nervous tissues, and bones, in which there is an overgrowth of the connective-tissue elements of those structures, the fibrous overgrowth being such that although it appears to be the result of the continued action of the syphilitic virus, yet it refuses to yield to the usual anti-syphilitic remedies. For this reason some authorities do not regard it as an integral part of the syphilitic attack, and it may more properly be regarded as an expression of the profound nutritional perversion of fibrous and other tissues which syphilis produces.

Etiologically syphilis is met with either as the acquired or the hereditary form. In the former case the disease is implanted by direct inoculation, in the latter case by inoculation of the fœtus through the placenta.

It is now generally thought that some form of micro-organism is the cause of syphilis, and Lustgarten has found bacilli similar in appearance to those of tubercle in the cells of gummata.

Acquired Syphilis in the Adult

The sites of inoculation are the mucous membrane of the genitals, lips, anus, or even, there is reason to believe, the unbroken skin of the finger, as following digital examinations. Feeding, and other contaminated utensils, have been known to be the means whereby the virus has been conveyed.

Course and symptoms.—After a period of incubation, lasting from fourteen to sixty-three days, the average being thirty-five days, the primary chancre appears at the point of inoculation as a red painless papule, which gradually enlarges until it forms an elevated sore, with steep, well-defined margins and flattened top. The base of the sore is much indurated, the induration being of a cartilaginous consistence, the tissues around sharing in this. This is the typical hard or Hunterian chancre, which, unless irritated, never suppurates. Its surface is often covered by a brown scab which arises from a clear serum-like secretion oozing from the surface of the sore. Many modifications of this typical chancre are met with, and it is often difficult to be sure of the identity of a lesion without awaiting the time necessary for the development of secondary syphilitic symptoms. In cleanly persons, and if the inoculation is on the glans penis, a "coppery" desquamating papule may be the only sign of the implantation of disease, and the typical Hunterian chancre does not follow. It is important to recognise such a variety as this, as it may be readily overlooked by the patient, and even by the medical man, so that the disease may be untreated in its earlier stages, when it is essential that thorough treatment should be carried out. It seems also that such chancres are sometimes followed by secondary symptoms of so slight a character as to pass unnoticed, but it is just in these cases that degeneration of the central nervous system and of the vessels often follows in middle life. In other cases the infection is of the mixed variety, *i.e.* the virus of "soft" and of "hard" chancre are implanted at the same time, and one or more of the soft chancres may heal, and then undergo the characteristic induration of syphilis, and a hard chancre ensues. The induration may be like a piece of parchment or a button let into the mucous membrane or skin. It lasts for a variable time, for about two to four months, and then the ulcer heals and a scar is left. In women chancres on the mucous membrane of the genitals are by no means so well marked nor so well defined as in men. The diagnosis of a typical hard chancre is not difficult, but the identification of the disease when the desquamating papule, or when soft chancres are present, and when the hard chancre has been irritated by caustics, so that it suppurates, is not easy. A chancre and herpes of the penis are sometimes confused.

From the seat of inoculation the virus spreads to the lymphatic glands of the groin and these become enlarged and hard. They are painless, non-adherent to the skin, and do not suppurate unless the chancre be irritated or be of the mixed variety, *i.e.* "hard" and

BERI-BERI

A specific peripheral polyneuritis, characterised by disorders of sensation, paresis, changes in the electrical response of the muscles and nerves, and widespread vasomotor disturbances of such a nature as to cause either a general anasarca or an atrophic appearance of the body. The disease is one of environment, and may become endemic in localities or abodes. It is usually attended by a high mortality, death resulting from exhaustion, paralysis of the heart, or of the muscles concerned in respiration.

Geographical distribution.—Originally described by Bontius in India, the disease has in recent years been scientifically studied in many tropical, sub-tropical, and even temperate climates, more especially in Japan, in Brazil, and in the Dutch East Indies. In addition to its occurrence in these several countries beri-beri is met with in the southern provinces of China, in Annam, throughout Malaya, Borneo, Fiji, New Caledonia, and even amongst natives of, and the Chinese immigrants in, Australia. In America it is found amongst the fishermen of the North Atlantic sea-board, in Havana, at Panama, in Brazil, and in the Sandwich Islands. In Africa cases have been met with from the neighbourhood of Lake Nyassa and the Congo (Manson). Lastly, attention has been drawn to the disease in several places in Europe, more especially in Ireland, where, in the Richmond Asylum, Dublin, during 1896, 1897, and 1898, a marked outbreak of the disease has been described by Dr. Conolly Norman.

Etiology.—The cause of beri-beri has not yet been ascertained. A bacterium was figured and described by Pekelharing and Winkler as the result of their investigations in Java and Sumatra, but the specific nature of the organism has not been confirmed by subsequent observers.

A diet deficient in nitrogen, such as rice, especially when the grain is of inferior quality and deprived of its outer covering, is by many competent observers held to be associated with outbreaks of beri-beri. The chief reason for this belief is that a change to a more nitrogenous diet is frequently followed by the disappearance of the disease. In the Japanese navy, where beri-beri (kakké) was very frequent, a change in diet of the kind indicated was followed by highly satisfactory results. There are several arguments against

rice being a direct factor in the etiology, none being more potent than the late peculiarly isolated outbreak in the lunatic asylum in Dublin. By some the disease has been ascribed to the consumption of certain species of fish imperfectly cooked.

Of other assigned causes there are many. Overcrowding, malaria, climate, anæmia, may furnish a favourable nidus for an outbreak of beri-beri by lowering the vitality and diminishing the bodily powers of resistance, but they cannot determine the onset of a disease of so specific a character. Beri-beri is essentially the disease of environment or habitation. It would seem as though a dwelling or ship became infected, and that the disease clung to the place. As a consequence healthy persons taking up their residence in quarters vacated by beri-beri patients readily become infected.

The evidence goes to show that beri-beri is dependent upon a toxic influence, probably parasitic in nature, having its habitat, in all probability, outside the human body. The disease is not regarded as directly contagious, nor is the beri-beric considered to be personally infectious. The writer, however, found what appeared to be direct communicability take place in a hospital for Chinese in Hong-Kong. A number of cases of beri-beri had been admitted to a general ward, and after a time beri-beri developed in several patients suffering from open sores in the same ward, whilst it passed over those who showed no wounds. Young men are most frequently the subjects of beri-beri, but with the exception of infants and octogenarians it has been known to attack persons of any age and of either sex. The rich as well as the poor suffer, but the disease is propagated and thrives in the overcrowded, insanitary native hovels, in the barracks where native soldiers congregate, in the ill-constructed, insanitary, and crowded temporary dwellings on newly-opened plantations. Beri-beri is also most frequently met with at low levels, and more especially, but by no means exclusively, along the sea-coast.

The Dutch observers in Sumatra established the fact that between the period of exposure and the development of clinical signs and symptoms of the disease, or, in other words, during **the incubation period**, careful investigation will show that there exist several latent signs. Of these the chief are a slight œdema along the crests of the tibiæ, and important variations in the response of the muscles and nerves to electrical stimuli. The minimum period of incubation of beri-beri is about five weeks. The maximum period may extend over several months.

Symptoms.—The "invasion" period of beri-beri—the "initial

phase"—presents the following signs and symptoms:—slight œdema along the tibial crests; pale and swollen-looking features; a slight rise in temperature, which may be very evanescent, lasting only a few hours, but nevertheless none the less constant; palpitation; a small, irritable pulse; some apparent increase of cardiac dulness; violent cardiac impulse; a prolonged first and reduplicated second sound; shortness of breath on exertion; difficulty in walking quickly and going up and down stairs owing to muscular stammering; circumscribed anæsthesia and pain on pinching the muscles of the lower extremities.

When beri-beri has developed there will always be found in the calf of the legs a patch which is insensible to a light touch, and to both galvanic and faradic currents. The leg muscles, and afterwards the muscles of the thigh, become painful when pinched, and the anæsthetic areas increase in extent. The muscles become weaker, their quantitative irritability is diminished, and very slight resistance is sufficient to stop extension of the leg and flexion of the thigh. The muscles of the calf, when contracted, bulge abnormally, but although painful to pressure there is seldom found any idio-muscular contraction, nor are they usually irritable to percussion. When the patient attempts to rise from his bed, or to lie down, considerable awkwardness is noticeable, and when he attempts to walk the gait is markedly abnormal. He wavers when he tries to stand with his eyes closed, nor can he stand on tip-toe, nor on one foot. During walking the patient raises the foot from the floor with difficulty, the toes leaving the floor last, and, after lifting the foot high and pushing it forwards, suddenly drops it on the floor. The dynamometer also shows that the muscular power of the hands and arms is distinctly lessened. As the disease progresses the anæsthetic areas in the legs may extend from the knee along the inside of the limbs to the heel; and the thenar and hypothenar eminences in the hands become anæsthetic, whilst as yet the parts of the hand beyond are unaffected. The muscular sense is undisturbed, the patient localises well and can imitate with one limb passive movements made for him with the other. The condition of the reflexes is characteristic. The knee jerk completely disappears, either from the onset of the initial phase or after a few days. Ankle clonus is absent, but the superficial abdominal and scrotal reflexes are readily elicited. The muscles, more especially those supplied by the external popliteal nerve, exhibit the reaction of partial degeneration. Irritability to the faradic current is suppressed, whether the current is applied directly or indirectly, and

there is also diminution of direct and indirect irritability to the galvanic current. The subsequent symptoms depend largely on the seat of the nerves attacked.

The dilated heart may give out, or this condition, combined with a sudden effusion into the pericardium, may cause cyanosis, dyspnœa, or syncope. The respiratory muscles, on the other hand, may become paralysed, causing sudden death by asphyxia. Vomiting is a grave sign, and death, when it occurs, is usually sudden. In favourable cases the œdema, if it exists, disappears, the paralytic signs are first stayed in their advance and then abate in their intensity. Power returns to the hands and legs, the irritability of the heart lessens, dyspnœa disappears, and after three months or so the patient is usually able to get about, or even follow his employment. Occasionally it happens that paresis remains for an indefinite period. During the development of these paralytic signs and symptoms the general health of the patient is wonderfully good. The digestive organs present nothing amiss, and the urine seldom betrays any signs of renal disturbance.

Varieties.—The three most pronounced types of beri-beri are the œdematous, wet, moist, dropsical; the atrophic, dry; and the mixed. In addition to these names, however, we are familiar with such terms as "acute" and "chronic" beri-beri, "foudroyante," etc. It is doubtful whether any one of these is worthy of the name of a variety, as it is possible the one is but the precursor or sequel of another, a mere predominant symptom being seized upon to constitute the basis of differentiation.

1. The *œdematous*, *dropsical*, "*wet*" *or* "*moist*" form of beri-beri is characterised by a fairly general œdema. The anasarca closely resembles that met with in a case of acute Bright's disease, but the urine, although presenting occasionally a slight albuminous cloud on boiling, shows none of the characteristic features consequent on acute nephritis. The œdema is at times partial, often missing the scrotum, and at times changing its site. The serous cavities may be the seat of a large amount of effusion, the pericardial cavity being especially liable to effusion; but the pleural cavities may be filled to such an extent that breathing is greatly hampered and the lung space so diminished that asphyxia supervenes.

2. The *atrophic*, "*dry*," *or purely paraplegic* variety of beri-beri is, as the names imply, associated with shrinking of the tissues of the body. The muscles are flabby and the fat of the body disappears. The patient, as regards his alimentary and renal condition, may

be pronounced healthy, and it is to a paralysis of the laryngeal or respiratory muscles that he usually succumbs.

3. *Atrophic and œdematous*—"*mixed*"—*beri-beri.*—When atrophic symptoms are obscured by serous effusion into the muscular and the connective tissues, and when, also, the serous cavities are the seat of a similar effusion, the clinician, pledged to the cognisance of a "wet" and a "dry" variety of beri-beri, will find great difficulty in referring the disease to its particular variety. Hence the adoption of the term "mixed," in which the signs and symptoms of the "wet" and "dry" varieties are combined.

In all these divergencies, however, one symptom remains constant, viz. the electrical modifications of the nerves and muscles. It would be well to dispense with these distinctions, except in so far as they indicate stages in the disease, because œdema is only a secondary phenomenon, and if the mixed form is taken as the type, the dropsical and dry forms are but a quantitative modification of it.

The motor disorders.—The most constantly paralysed muscles are the groups supplied by the external popliteal nerves, viz. the peronei, and the extensors of the toes; the next most frequently affected muscles are the flexors of the toes. The extensors of the knee and the gluteal muscles are also liable to be involved in the paresis, whilst the adductors and the knee flexors escape. In the upper extremities the extensors of the hand and fingers, the supinator longus, the triceps, the flexors of the hand and fingers are, in the order given, the muscles liable to attack. In addition to these the abdominal muscles, the diaphragm, and the intercostal muscles suffer. Even the muscles supplied by the cranial nerves may become involved; the muscles of expression and the muscles of the eyeball having been known to become paralysed. The laryngeal muscles are also frequently involved, with the result that sudden death ensues from asphyxia.

Disorders of sensory nerves.—The sense of touch is first lost on the inner aspect of the calf of the leg, then on the dorsum of the foot, and finally sensation may be lost everywhere below the knee. In the upper extremities sensation disappears first on the anterior aspect of the wrist, then over the thenar and hypothenar eminences, and finally over other parts of the hand; the ends of the fingers being the last places from which it vanishes. Anæsthesia may overtake the whole of the upper limb as far as the shoulders. Anæsthetic areas may also be met with over the anterior aspect of the trunk, reaching as low as the umbilicus.

Heart affections.—The heart is early affected in beri-beri. Not only are there marked subjective symptoms, but there is a pronounced enlargement of the cardiac area, especially towards the right, and pathological evidence shows that there is hypertrophy accompanied by dilatation of the right ventricle. The state of the ventricle explains the dropsical effusion into the tissues and the serous cavities and the other effects of venous obstruction.

Post-mortem appearances.—According to the type of beri-beri which has proved fatal, so do the post-mortem evidences vary. In the "wet" variety serous effusions may be found in the subcutaneous and intermuscular tissues and in the serous cavities of the body; in the "dry" variety, on the other hand, the muscles when cut into reveal the yellowish-brown colour characteristic of atrophy. It must be remembered, however, that œdema to some extent has always existed at some period of the disease, and pericardial effusion in particular is one of the most constant features of beri-beri. It is in the heart itself, however, that pathological change is to be sought for. Hypertrophy of the right ventricle is always present, accompanied by a dilatation varying from, it may be a small, to an enormous extent. The heart muscle is often pale, but microscopic examination shows that this is not usually due to fatty degeneration. Of the other organs the lungs may be œdematous, the liver congested, the spleen increased in bulk and weight, and the blood in the large veins in a fluid state. The examination of the nervous system shows that, in the nerves generally, a state of peripheral neuritis and nerve degeneration exists, and that the lesion diminishes in intensity as the centre is approached. The anterior roots of the spinal nerves show no pathological change, but in the posterior roots, more especially in the part between the ganglion and the nerve trunk, atrophied fibres are met with. In the central nervous system the most constant change is an alteration (it may be an atrophy) in the large cells occupying the anterior cornua of the spinal cord.

Prognosis.—During an attack of beri-beri it is well-nigh impossible to venture on a prognosis; for cases of seeming mildness prove fatal, whilst cases of apparently a severe type recover. In general about 20 per cent of those attacked die; but the numbers vary, it may be as much as 10 or even 15 per cent either way. Unfavourable signs are: cardiac and vascular changes, such as a quick and feeble pulse, epigastric pulsation, throbbing of the blood vessels in the neck and increase in the cardiac area; extensive serous effusions into the peritoneal, pleural or pericardial cavities; failure

in power of the respiratory muscles; marked diminution in the quantity of urine passed; and vomiting. The last-mentioned feature supervening, as it sometimes does during the course of an acute attack of beri-beri, is a very unfavourable sign.

Diagnosis.—Beri-beri has to be diagnosed from peripheral neuritis, due to alcohol or to malaria, from locomotor ataxy, and from epidemic dropsy. In epidemic forms of the disease the diagnosis is readily enough arrived at, but when sporadic cases, or when even limited outbreaks occur in what are regarded as non-beri-beric countries, as in Ireland, the recognition of the disease is attended by obvious difficulties. Reliance must be placed upon the presence of œdema, limited, it may be, to the front of the shins; upon the absence of knee jerk; upon the tumbling action of the heart; pain on pinching the limb muscles and patches of anæsthesia on the legs and perhaps the arms. If electrical testing is available the diagnosis is greatly facilitated.

Treatment—*Prophylaxis.*—Seeing that beri-beri is a disease of environment it is necessary to correct or alter the immediate surroundings of those exposed to the disease. Disinfecting the abode, the furniture, and the clothing of beri-berics serves to check the numbers of those attacked; but it is only by evacuating the premises, and it may be leaving the locality where beri-beri is endemic, that an outbreak, say, amongst troops in barracks, coolies in coolie quarters, and prisoners in a jail, may be stamped out. In the case of the individual it is only by removal to an untainted locality that a cure can be confidently hoped for.

Rest in bed ought to be insisted upon and sudden movement or exertion forbidden. The diet must be liberal in the item of nitrogenous elements, and if rice has been the staple food heretofore it should be supplanted by bread, meat, milk, and fresh vegetables. When it is impossible to immediately quit the abode, as on board ship, those afflicted with beri-beri should be granted the best sleeping accommodation possible, and during the day should be brought out into the open air.

The state of the heart and of the circulatory organs generally calls for medicinal treatment. Cardiac stimulants, such as digitalis, may be administered with good effect; nitroglycerine in the form of the liquor trinitrini (1 min.), or tabellæ nitroglycerini B.P. (1 tablet) should be at hand for emergencies of cardiac failure. Amyl nitrite may be inhaled from a crushed capsule with the same intention. The functional condition of the heart in beri-beri is so little understood that it is difficult to justify, far less to explain the beneficial

action of these drugs, except it be that by the administration temporary relief is afforded to the enlarged right ventricle, by diminishing the resistance of the blood vessels to the onward passage of the blood.

Aspiration of first one, and (if necessary) later the other pleural cavity affords relief in dyspnœa, and the writer found benefit by venesection in one case of threatened asphyxia and by aspiration of the pericardial effusion in another.

When the patient is convalescing strychnine is the best medicinal tonic; but massage, electrical stimulation and general tonic treatment favours recovery. It was at one time believed that beri-beri always relapsed, and that in about twelve months a recrudescence was to be looked for. No doubt this is the case when the patient returns to an infected environment, but by residence in a healthy locality such a relapse may be almost certainly avoided.

James Cantlie.

EPIDEMIC DROPSY

An epidemic disease of variable mortality and lasting from three to six weeks; characterised by œdema of the lower extremities or of the entire body, accompanied by pyrexia, by gastric and intestinal irritation, by aching in the limbs and trunk, and frequently by a cutaneous rash of a rubeolar appearance.

Geographical distribution.—Since Dr. Kenneth M'Leod first described the disease in Calcutta in 1877, several observers have recorded outbreaks of the disease. In Assam, in Lower Bengal, and in Mauritius, well-defined occurrences have taken place, and, in all probability, outbreaks of this particular malady have developed at several places on the littoral of the Indian Ocean.

Etiology.—Epidemic dropsy appears to be communicable from one member of the community to another, and is mainly confined to the adults of both sexes of a family. It occurred in Calcutta during the cold weather, disappeared completely during the hot season, and for three successive winters, 1887 to 1890, recurred persistently; since then the disease does not seem to have re-appeared. No European is known to have contracted the disease.

No bacteriological investigations have been as yet communicated concerning the causation of epidemic dropsy.

Symptoms.—Initial symptoms vary. In some instances the disease is ushered in by the dropsical effusion; in others, fever first attracts attention; or again general malaise or intestinal flux precede all other manifestations.

The œdema appears in the feet and ankles and may extend beyond the lower extremities to the whole body, sometimes lasting for a considerable period. Pleural and pericardial effusions have sometimes been noticed. Fever may usher in the symptoms, may accompany the dropsy or appear only during its subsidence. It is seldom the thermometer registers higher than 102°. Vomiting is seldom distressing; diarrhœa or even dysentery of a mild type occasionally occurs. In addition to itching and burning of the skin, a general exanthematous rash, of a rubeolar character, is a common, but by no means a constant, accompaniment. The general signs and symptoms include a weakened pulse, breathlessness, and marked anæmia and prostration. Nocturnal pains in the limbs have been frequently observed.

Occasional signs and symptoms of pneumonia, œdema of the lungs, cardiac dilatation, scurvy, and albuminous urine have all been recorded as complications of the disease.

Diagnosis.—The only disease likely to be confused with epidemic dropsy is beri-beri. In fact many observers positively assert their identity; whilst on the other hand it is possible, nay probable, that many cases at present classed as beri-beri will prove to be of the nature of epidemic dropsy. The one characteristic feature of beri-beri which serves definitely to stamp its specific nature is the nervous and paralytic affections, and these are absent in epidemic dropsy. Moreover, beri-beri is more chronic and never complicated by a cutaneous eruption, nor is fever a prominent feature.

Mortality.—In the Calcutta epidemics a death-rate of from twenty to forty per cent of those attacked occurred. On the other hand, in the Assam outbreak, no fatal cases were known.

Treatment.—Such remedial treatment as a weakened circulation demands, and as is appropriate in urgent cases of dyspnœa or apnœa is called for in the treatment of epidemic dropsy.

Southey's trocars are indicated as a means of relieving the dropsical effusion, and even aspiration of the pleura or pericardium may be necessary. During convalescence anæmia is the most prominent condition which requires treatment.

JAMES CANTLIE.

ORIENTAL SORE

Syn. Delhi Boil; Bagdad Sore; Biskra Button; Aleppo Evil

A specific inflammatory affection of the deeper layers of the skin, which, commencing as a papule, soon crusts over, and spreading by phagedæna, develops an ulcer of an indolent character. The healing is protracted, and a permanent scar, a "date" mark, remains to indicate the seat of the affection.

Geographical distribution.—The various synonyms indicate the principal places in which this peculiar affection is met with. In Europe, Greece and Crete seem to be the only countries in which the disease has been noted. In Africa it occurs in Morocco, Egypt, and certain parts of the Sahara. In Asia: Bagdad in Mesopotamia, Aleppo in Syria, Delhi and Mooltan in India, are the chief seats of the disease. But Arabia, Persia, and Turkestan are known also to harbour the malady. Some ten years ago persons residing in the town of Bahia, Brazil, were declared to be affected with true "Oriental Sore."

What the specific infective matter may be is unknown. Objects that appear to be minute parasites in the "boil" have been described by Dr. Smith as the ova of Distoma, by Dr. V. Carter as the spheroids and mycelium of a special parasite, and by Dr. Cunningham as zoocysts or sporocysts which are also met with in the water in some of the districts where Oriental sore is endemic. Biting insects are in all probability the carriers of the infectious matter, as it is the exposed parts of the body that are almost solely attacked.

Etiology.—It would seem as though a special state of climate and constitution were necessary for the development of the disease, as it occurs in countries possessing for the most part a dry, even arid, climate, and it appears towards the end of the hot season, when the vigour of those attacked is probably at its lowest. Insanitary surroundings favour the development of Oriental sore. All nationalities, both sexes and all ages, are liable to attack, and the disease seems to occur in special prevalence, not only at certain seasons, but also during certain years.

One attack as a rule confers a permanent immunity.

Communicability.—The disease is not confined to human beings. Dogs and horses are stated by Fayrer to suffer from a

disease in India closely resembling Oriental sore. Both man and the lower animals can be inoculated by discharge from the surface of ulcers. Attempts at inoculations from cultures of certain micrococci obtained from the centre of the papules have hitherto failed.

Symptoms.—On some exposed part, or parts, of the body, usually the face, neck, or extremities, the attention of the patient is drawn to a small itching papule, or to a number of similar pimples on different parts of the body. When looked at carefully the papule appears pink in colour; it is frequently situated around a hair follicle, and the epidermis over it is seen to be dry and loose. Gradually the subcutaneous tissues around become infiltrated and feel boggy to the touch; the intense itching alternates with occasional stinging pains; and a slight oozing from the surface and moistening of the skin causes the epidermal cells to cake, and finally to crust. Underneath the crust an ulcerating surface develops, at first quite superficially, but gradually the ulceration extends deeper and wider, presenting a rather sharply cut and indurated edge. The crusts fall and re-form from the thin ichorous material which exudes. Around the primary papule others form, and, as these coalesce, they add to the extent and intractability of the sore. An individual sore is usually about one inch in diameter, and there may be several on different parts of the body. It is believed also that any ordinary boil or wound may take on the characters peculiar to Oriental sore. After many weeks, or more likely months, the wound shows signs of healing. Slow in its development, however, the "sore" is still slower in its disappearance, and it leaves behind the peculiar "date" scar, indelibly impressed. The cheek and nose are favourite sites of the disease, and a large "date" mark on either of these may be followed by permanent unsightliness.

Prognosis.—There is but little danger to life from Oriental sore. Were the wound to be attacked by erysipelas, or become markedly phagedænic, alarming symptoms might ensue.

Treatment.—Destruction by caustics or cautery of the primary seat of infection has been frequently attempted, but the results are not encouraging; and in the absence of any known specific application, it is wiser to pursue an expectant treatment, viz. attending to the general health, seeing to the sanitation of the house and environment, applying soothing antiseptic remedies to the sore whilst it is indurated and irritable, and promoting healing by cleansing the wound and protecting its surface.

JAMES CANTLIE.

VERRUGA PERUANA

A specific, general, infective, inoculable disease, characterised by constitutional symptoms and a special granulomatous eruption. It seems to be quite distinct from frambœsia.

The disease is peculiar to certain defiles penetrating the tropical Andean mountainous districts of the departments of Ancache and Lima, which are watered by rivers overflowing each January and June. There are no limitations as to age, sex, or race. Domestic animals, such as dogs, pigs, fowls, turkeys, horses, mules, llamas, cows, and asses contract the disease, which assumes remarkable proportions in the solipeds.

Eight to forty days are generally allowed to be the **incubation period**; some observers give even a longer range.

The **invasion** symptoms may be of very different degrees of severity. The malady may be so intensely virulent that the patient succumbs before the eruption appears. Usually there is an insidious onset with general malaise, which gradually becomes intensified. Pain and fever are prominent. Rheumatoid pains, with nocturnal exacerbations, shift from joint to joint, and are often terribly severe. Muscular pains, also, may produce rigidity and contractions. A great variety of febrile types are observed, of which the acute arthritic and low typhoid may be especially noted. The fever may be intermittent, and is generally hectic; the intensity corresponds with the virulence of the infection. A marked anæmia sets in, with profound prostration, and these states are apt to be increased by the subsequent ulceration and bleeding of the eruption. Hæmic murmurs may develop, serous effusions are frequent, and the spleen, and sometimes the liver, enlarges. The *eruption* appears after a period of twenty days, or only after six or eight months, or even one year, it is said, and when it evolves the general symptoms tend to abate. Its duration may be put at about two to eight months, but varies widely according to the number of outbursts, and the quantity and volume of the elements and attending complications. It appears usually in the skin of the extremities and face, and spreads thence to more or less of the rest of the body, and to the mucous membranes, and even the splanchnic organs and serous membrane. The distribution is, however, most variable. The eruptive elements may be small and superficial, or develop more deeply in the cutis

and subcutaneous tissue, and then attain the size of an orange, or more, and give rise to grave cachexia by their sloughing and bleeding. The smaller type begins as a tiny red spot, which develops into an itching, shining papule, and finally into a very vascular, red "wart" (whence the name *verruga*), which may become pedunculated. The eruptions gradually die away with exfoliation or bleeding, or ulceration and crusting. *Histologically* the granulomata are said to bear a striking resemblance to sarcomata, and to be specially characterised by a remarkable vascularity. According to Yzquierdo, they are caused by a specific bacillus, which is found between the cells, and also thrombosing the vessels.

The **diagnosis**, in the pre-eruptive stages from malaria, rheumatic and typhoid fevers, is often very difficult. Verruga is a very serious and dangerous affection.

There is no specific **treatment** known to be effective. The sufferer should be removed at once to as healthy a locality as possible at the sea level.

T. Colcott Fox.

FRAMBŒSIA

A highly contagious, but not hereditary, specific, general, chronic, infective disorder, characterised by a cutaneous granulomatous eruption of special aspect, resembling a raspberry, whence the name is derived through the French "framboise." It is endemic in some of the West Indian Islands ("yaws"), especially Dominica; in parts of Brazil and the Spanish South American colonies ("bubas") and Guiana; in Fiji ("koko"), Loyalty, New Caledonia, and other Melanesian Islands; in Ceylon ("paranghi"), along the Coromandel Coast, Assam, and the East Indies; in the Moluccas, the East Coast of Africa, along the Mozambique Channel, and on the West Coast about Sierra Leone. One attack renders the subject immune for the most part. It is not syphilis altered by race, climate, and locality, for both diseases breed true in the same community; syphilis can be inoculated and run a typical course in a yaws subject, and healthy children are born of women actually, or recently, suffering from yaws. Moreover, the incubation stages are different, and many of the secondary symptoms characteristic of syphilis, such as iritis, sore throat, and usually the adeno-

pathy, are absent. Tertiary symptoms do not follow, it is said, though ulceration is not unfrequent.

Inoculation occurs through any of the breaches of surface, so frequent in unclothed people living under unhygienic, crowded, miserable conditions.

After an **incubation period**, variously stated from two to ten weeks, or a somewhat shorter average time (twelve to twenty days) in experimental inoculations, an *initial papule* appears at the seat of inoculation in a considerable proportion of cases, though not invariably, and develops into a moist, yellow, fungating granuloma, similar to those of the generalised eruption, and sometimes persisting for a long period as the "mother-yaw." Simultaneously with the initial papule, or shortly after, but usually within ten days, a granulomatous, more or less generalised, eruption appears in successive crops, and may last as a whole from three months to four years, averaging about two years. The eruption evolves as itching papules, the size of pin-heads, which may abort in the early stages with the separation of corresponding scales. Some authors draw special attention to the occurrence of such furfuraceous desquamation in the earlier stages of the effection or at later periods. As a rule the enlarging papule bursts through the epidermis and discloses a central, yellowish, softened point which may simulate a pustule. Finally, an abruptly-raised, painless excrescence is formed like "proud flesh," or somewhat resembling mucous tubercles or condylomata, or, in certain rarer dry states, warts. These efflorescences may reach the size of a small pea, or even a walnut, and may form larger patches by confluence, or become annulate. They tend to be covered with a thin scab, and on disappearance after some weeks leave a stain lasting a few or many months. In many cases successive crops continue to appear. The eruption may be generalised and copious, or scanty and localised. The lips and nostrils may be implicated, but otherwise the mucous membranes appear to escape, as do the viscera. In the conditions under which framboesia occurs it is not surprising that secondary ulcerations should result in many cases. The causal micro-organism has not yet been definitely established.

Constitutional symptoms, such as fever, are absent, slight, or rarely severe, and, as a rule, the subjects continue their usual avocations.

Treatment.—Isolation is necessary to prevent the spread of the disease. In ordinary cases, where the general health is good, the disease runs its natural mild course under proper feeding and hygiene, and the prognosis is most favourable. Mercury and iodide

of potassium have been much used, and the reports as to their action are most conflicting. The local application twice daily of chromic acid, or a mixture of picric and carbolic acid to dry up the granulomata is recommended; and for some of the later and more persistent lesions nitrate of silver and sulphate of copper are useful.

T. Colcott Fox.

SYPHILIS

Syphilis is a specific contagious disease, communicable by direct inoculation. Its course is characterised by a primary lesion (chancre), by early constitutional (secondary) symptoms, and by late constitutional (tertiary) symptoms.

Frequently a final stage is to be observed, a post-syphilitic fibrosis, especially well marked in the blood vessels, nervous tissues, and bones, in which there is an overgrowth of the connective-tissue elements of those structures, the fibrous overgrowth being such that although it appears to be the result of the continued action of the syphilitic virus, yet it refuses to yield to the usual anti-syphilitic remedies. For this reason some authorities do not regard it as an integral part of the syphilitic attack, and it may more properly be regarded as an expression of the profound nutritional perversion of fibrous and other tissues which syphilis produces.

Etiologically syphilis is met with either as the acquired or the hereditary form. In the former case the disease is implanted by direct inoculation, in the latter case by inoculation of the fœtus through the placenta.

It is now generally thought that some form of micro-organism is the cause of syphilis, and Lustgarten has found bacilli similar in appearance to those of tubercle in the cells of gummata.

Acquired Syphilis in the Adult

The sites of inoculation are the mucous membrane of the genitals, lips, anus, or even, there is reason to believe, the unbroken skin of the finger, as following digital examinations. Feeding, and other contaminated utensils, have been known to be the means whereby the virus has been conveyed.

Course and symptoms.—After a period of incubation, lasting from fourteen to sixty-three days, the average being thirty-five days, the primary chancre appears at the point of inoculation as a red painless papule, which gradually enlarges until it forms an elevated sore, with steep, well-defined margins and flattened top. The base of the sore is much indurated, the induration being of a cartilaginous consistence, the tissues around sharing in this. This is the typical hard or Hunterian chancre, which, unless irritated, never suppurates. Its surface is often covered by a brown scab which arises from a clear serum-like secretion oozing from the surface of the sore. Many modifications of this typical chancre are met with, and it is often difficult to be sure of the identity of a lesion without awaiting the time necessary for the development of secondary syphilitic symptoms. In cleanly persons, and if the inoculation is on the glans penis, a "coppery" desquamating papule may be the only sign of the implantation of disease, and the typical Hunterian chancre does not follow. It is important to recognise such a variety as this, as it may be readily overlooked by the patient, and even by the medical man, so that the disease may be untreated in its earlier stages, when it is essential that thorough treatment should be carried out. It seems also that such chancres are sometimes followed by secondary symptoms of so slight a character as to pass unnoticed, but it is just in these cases that degeneration of the central nervous system and of the vessels often follows in middle life. In other cases the infection is of the mixed variety, *i.e.* the virus of "soft" and of "hard" chancre are implanted at the same time, and one or more of the soft chancres may heal, and then undergo the characteristic induration of syphilis, and a hard chancre ensues. The induration may be like a piece of parchment or a button let into the mucous membrane or skin. It lasts for a variable time, for about two to four months, and then the ulcer heals and a scar is left. In women chancres on the mucous membrane of the genitals are by no means so well marked nor so well defined as in men. The diagnosis of a typical hard chancre is not difficult, but the identification of the disease when the desquamating papule, or when soft chancres are present, and when the hard chancre has been irritated by caustics, so that it suppurates, is not easy. A chancre and herpes of the penis are sometimes confused.

From the seat of inoculation the virus spreads to the lymphatic glands of the groin and these become enlarged and hard. They are painless, non-adherent to the skin, and do not suppurate unless the chancre be irritated or be of the mixed variety, *i.e.* "hard" and

they often stand apart and slope towards each other, they are pegged, *i.e.* they are broader near the gum than at their free edge, and they are notched from the breaking away of the central portion of the free edge. The other mentioned teeth, too, are often dwarfed and ill-developed, but lack the characteristic features of the central incisors. Incurable nerve deafness, affecting both ears and of sudden onset, may also occur as a later sequela. Associated with the deafness, or independently of it, there is often headache of a very intractable nature. A subacute symmetrical synovitis of the larger joints, most usually the knees, attended by little or no pain, is very rare apart from inherited syphilis. The only skin affection in the later stages is the gummatous infiltration of the skin and subcutaneous tissues known as "syphilitic lupus." This consists usually of somewhat large patches of inflammation and hardening of the cutaneous tissues, breaking down in some places into deep ulceration, and healing in others with persistent serpiginous scarring. Interstitial keratitis is seldom seen before the age of seven years, and is commonest between this age and puberty, but may come on at the age of twenty or later. Both eyes are invariably affected, but one is usually attacked before the other. Iritis is occasionally met with. Nodes on the long bones, and gummata in the skin, abdominal viscera, and the brain and elsewhere, may appear at any age after infancy, but are commonest at the times when interstitial keratitis usually appears. One case, at least, is on record where, in addition to nodes, there was a diffuse osteitis of the right tibia, leading to partial gigantism of the limb. In older children, usually at the age of puberty, gummata may occur in the tongue and soft palate, and, breaking down, may lead to perforation and destruction of the last. Care should be taken, however, to make sure that such cases are not of the acquired disease, as this, unfortunately, is by no means a rarity in children. Syphilitic orchitis occasionally occurs soon after infancy, but is commonest at the usual times of the later manifestations. Lardaceous disease is almost unknown at any stage of the inherited complaint, but it is quite conceivable that it might occur in the rare event of suppurative bone lesions of long persistence. In a few instances locomotor ataxia, commencing at the early age of puberty, has followed on inherited syphilis in infancy, and it is stated by some alienists that general paralysis of the insane, when developed in early life, is invariably attributable to this cause.

It must be strictly remembered that, with the exceptions of

Hutchinsonian teeth and interstitial keratitis, any of the above-mentioned later manifestations of inherited syphilis are very exceptional in occurrence.

Acquired syphilis in infants.—From the nature of things, acquired syphilis is of necessity an extreme rarity in infants. As with adults, it can only occur through the agency of a primary chancre, and the periods of primary and secondary incubation are the same at all stages of life. Acquired syphilis in infants does not differ materially in its manifestations from the same complaint in adults, although it markedly does so from the inherited form in many respects. In the acquired syphilis of infants there is an absence of the bony affections of the skull, the early involvement of the abdominal viscera, and the specific epiphysitis, all of which are frequent and characteristic of the inherited form, and marasmus and snuffles are much less prominent features in the former than in the latter complaint. The throat and fauces are affected in the same manner, and at the same time, in the infantile acquired form as in the adult one, and the usual eruptions are the same in both. The eruptions, too, are chiefly manifested over the front of the trunk and flexor surfaces of the limbs, and show no peculiar predilection for the buttocks and chin, as in the inherited form. A marked feature of the acquired form in infancy is the scanty development and evanescent nature of the eruptions, and the early and luxuriant growth of condylomata. The power of infecting the healthy, moreover, is vastly greater in the acquired than in the inherited form in infancy.

Diagnosis.—The diagnosis of acquired syphilis in infants is precisely the same as in adults. That of inherited syphilis is perfectly simple in the majority of instances; the marked snuffling, the character of the eruptions, and their peculiar selection of sites leave little room for error or doubt. The snuffles may long precede any other symptom, and cases of marked and persistent snuffles, even with a total absence of all other signs, are most probably due to syphilis. Obstinate and progressive wasting, especially if unassociated with any obvious digestive disturbance, is not very unfrequently the only objective sign of the inherited complaint. The diagnosis in some of these last cases may be supported by the peculiar "café-au-lait" tint of the skin which, as Henoch has pointed out, is confined to the marasmic cases, and not to those of syphilis in general, as Trousseau supposed. In some cases pseudo-paralysis or epiphysitis may be the first symptom to call attention to the

malady, and in others, but very rarely, enlargement of the spleen may furnish the only evidence of it. A single well-formed mucous tubercle, or condyloma, is absolutely pathognomonic of syphilis. The family history as regards miscarriages and snuffles and rash in the older children is of prime importance, as it may help to confirm the diagnosis in the better marked cases, and in the more doubtful ones it may furnish evidence of more value than the existing clinical signs. Even after the intelligent use of all available criteria, there still remains a large class of cases in which the diagnosis is a matter of doubt. In such cases snuffles, rash, and other symptoms may be so ill-developed, and the family history so dubious, that a confident diagnosis is only possible with the self-sufficient. Here recourse may be made to the effect of treatment. Many such doubtful cases, it is true, improve and recover under the administration of mercury. But it must be remembered that many infants who are not syphilitic improve under mercury, and in the case of syphilis, as in other diseases, a diagnosis founded upon the mere effects of treatment can never be one that is quite satisfactory or convincing.

Prognosis.—In cases presenting signs of the disease at birth the prognosis is all but fatal. It is equally so in those in which jaundice or pemphigus supervene. Wasting dating from birth is seldom, if ever, recovered from, and the prognosis attaching to wasting in later months is scarcely more hopeful. Unfavourable signs are an early appearance, or extensive development, of the eruption, and any undue enlargement of the abdominal viscera. Cases where the rash is pustular from the onset generally die. Of the rest of the cases, if the infant be well nourished, and if the symptoms have not appeared before the beginning of the second month, the prognosis is good. As regards the future, too, it is only a small minority of those surviving the stage of infancy that present signs of the complaint in later years. Children, however, who have seemingly recovered from inherited syphilis are much more prone to succumb to the stress of other disorders than those less heavily handicapped at the start of life.

Treatment.—The essentials of treatment are comprised in the maintenance of nutrition and the due administration of mercury. For the first of these it is a bounden duty that the mother should, if possible, suckle her infant. If she be seemingly healthy, the small chance there may be of her contracting the disease from her infant by suckling it ought to be incurred. The great mortality amongst syphilitic infants lies largely amongst those that are hand-fed, and the difference between suckling and hand-feeding means

possibly one between life and death for many an infant. When the mother cannot suckle it, the infant must be either wet-nursed or hand-fed. The questions as to the dangers incurred by a healthy wet-nurse, and the details involved in a proper system of hand-feeding, are too lengthy for discussion here. It cannot, however, be too emphatically asserted that a proper diet is equally important with the drug treatment of the complaint.

For the second essential in treatment, the administration of mercury, only two methods need be considered, that of giving it by the mouth, and that by inunction. The former has two strong recommendations in its favour—simplicity and efficacy. The usual preparation given is the ordinary grey powder, and this generally meets all the requirements of most cases. It can be given in doses of one grain three times a day to infants of all ages. Given in these doses it rarely, if ever, causes diarrhœa, and if the latter supervene, it is generally due to some error in diet, or to the fact that the complaint is epidemic at the time. When diarrhœa is present, each dose of the grey powder can be combined with a third or half of a grain of Dover's powder, according to the age of the infant. If in spite of this addition the diarrhœa should persist, or if it be considered that the internal administration of mercury causes digestive disturbance, then recourse can be had to the method of inunction. In this last, from twenty grains to half a drachm of mercury ointment should be rubbed into the inner sides of the thighs or the axillæ, or upon the surface of the belly binder, once a day. Under such a treatment it is undoubted that the eruptions and other manifestations of the disease rapidly disappear. The amount of mercury absorbed by the skin, however, is an uncertain quantity, and some observers believe that more infants treated by inunction come back in later months presenting symptoms of the disease than is the case with those who have been treated with mercury by the mouth. If this be so, then the method of administration by the mouth should have preference, unless otherwise contra-indicated, over that of inunction. Whichever method be adopted, the treatment should be faithfully carried out for a course of at least four months' duration, and longer if any symptoms are present. The fear of causing symptoms like those belonging to the salivation of adults can be dismissed; such salivation is practically unknown in infants.

Except in the rare contingency of nodes or gummata being present, there is no need of any addition of the iodides to the mercury given. The iodides merely assist in the more speedy removal of such complications, and have no real power in the way

of curing the disease. For this last, mercury is all essential at all stages.

If the nasal discharges cause blocking, a two per cent solution of the oleate of mercury, or a little dilute ammoniated mercury ointment, should be passed into the nostril with a camel's hair brush. Condylomata should be dusted with calomel, and if long persisting, be lightly touched over with one of the ordinary caustics. In the event of ulceration of any moment occurring, then the mercury given should be supplemented by doses of opium appropriate to the age of the child. In all the ulcerative conditions of infancy, syphilitic or otherwise, there is no drug, perhaps, of such value as opium.

J. A. Coutts.

RABIES

Syn. Hydrophobia

An acute infective malady of the central nervous system, the symptoms being dependent on the action of a poison which is developed throughout these organs, but more especially in the medulla.

Rabies or hydrophobia is a disease that is sometimes very prevalent in animals, and is occasionally seen in man. The name of rabies is usually restricted to the disease in the former, and the term hydrophobia used for the same malady in man. Hydrophobia is, however, a misnomer, since there is, strictly speaking, no fear of water, but only a difficulty in swallowing, more marked with liquids than with solids.

Occurrence in animals.—Rabies is most prevalent in dogs, cats, wolves and foxes; it is occasionally seen in horses, very rarely in pigs, and several outbreaks have occurred in deer. The frequency of rabies in the carnivora is associated with the fact that it is usually propagated by biting.

It is met with both sporadically and in epidemics, and frequently the latter can be traced to foci of the disease in certain parts of the country where it may be more or less endemic, and at intervals affecting large numbers of animals over wide tracts of country. In certain districts it is unknown, as, for instance, in Norway and Australia. It is rare in Germany, but it is more common in France

and Russia, and also in the East. In this country the incidence of the malady varies considerably; in the years 1895 and 1896 there was an extensive outbreak, but at the present time, 1899, the disease has greatly diminished in amount.

Virus of rabies.—The virus of rabies is remarkable in the fact that it is distributed throughout the nervous system, central and peripheral. In addition to this it is found in the secretion of certain glands, such as the salivary (especially the parotid), the lachrymal, the mammary, and the pancreas. The virus is not found in the blood, tissues, urine, nor in other excretions. When the malady is fully established, and *a fortiori* at death, it is found throughout the nervous system; in the earlier stages of the disease, however, it is limited to the medulla. The virus of rabies is comparatively readily destroyed by the action of sunlight, by heat, by dessication, and by the action of powerful antiseptics. Putrefaction destroys its activity more slowly, and the carcase of an animal dead from rabies has been found virulent as long as forty-five days after burial.

Mode of infection.—Rabies is usually communicated both to animals and to man by the bite of the rabid animal infecting the wound by means of the saliva. It is for this reason that hydrophobia is more frequent after bites on exposed surfaces, such as the face and hands, than when the person is bitten through clothes. Similarly animals covered with fur are less liable to contract the malady when bitten than shaved animals, or animals destitute of fur. The disease is not communicable from one animal to another by the carcase of the rabid animal being eaten by another. It is probable that infection is more readily conveyed if the injury involve a nerve, as it has been shown that the virus travels along the nervous system from the periphery to the centre. Thus, if the spinal cord be experimentally divided in the mid-dorsal region, and inoculation of the virus of rabies be made in the posterior half of the body, the lower segment of the spinal cord will contain the virus at a time when the upper half is free from it. From this it is held that the virus is propagated through the nervous system, and is not conveyed from the peripheral to the central nervous structures by the lymph or blood. Deep lacerated wounds involving the muscular planes are more liable to be followed by rabies than superficial wounds involving the skin and subcutaneous tissue. It is estimated that in the human subject from 16 to 25 per cent of persons bitten by rabid animals contract hydrophobia, the others escape for various reasons, but more especially from the clothes, boots,

etc., preventing the inoculation of the wound. Bites inflicted by a rabid wolf or cat are more liable to communicate the disease to man owing to the greater likelihood of the exposed parts of the body being bitten.

The incubation period of rabies varies greatly. In man it is usually six weeks, but it has been asserted that it may be as short as three weeks, and as long as twelve or eighteen months; in some quite exceptional cases an incubation period of from two to five years has been described. In animals the incubation period varies with the species. Thus in dogs it ranges from fifteen to sixty days, and in at least 50 per cent it is less than a month, whilst it is rare after 120 days. In cattle the incubation period varies from one to three months. In the rabbit it is usually fourteen to nineteen days. The variation in the duration of the incubation period depends to a great extent on the degree of virulence of the poison, and in street rabies, *la rage des rues*, there are great individual variations. In the laboratory, however, by transmitting rabies from one animal to another by inoculation, it is possible to elaborate a virus in which the incubative period, at any rate in the rabbit, becomes fixed at seven days.

Symptoms.—During the incubation period, both in animals and man, there is but little to be noted, and usually the wound heals with no symptoms of general disturbance. At the end of the period of incubation the site of the wound becomes irritable, and tingling and itching may be noticed, and in man it has been asserted that the wound may open up again. Soon both in animals and in man restlessness, agitation, and nervousness become marked. The subsequent course of the malady depends on which of two types it assumes. The most common clinical type is that known as "furious rabies," and in this condition *in the dog* or other animal the agitation and restlessness become increased, and the animal suffers from hallucinations; at this time, however, it is not savage, and it does not show any tendency to attack those near. Soon the bark becomes altered, exceedingly prolonged, high pitched, and, to a certain extent, stridulous. The seat of the bite, from being irritable, becomes anæsthetic, and it is not uncommon for the animal to inflict on itself severe wounds by gnawing the part. Some difficulty is experienced with deglutition, more especially with liquids; the restlessness leads the animal to wander about, and even to travel long distances, although at the onset of the malady it may have shown a tendency to withdraw itself from observation by hiding in dark corners. The animal

now rapidly becomes furiously maniacal, attacking animate and inanimate objects, and biting and swallowing at this period all sorts of foreign bodies, such as pieces of wood, bone, coal, rugs, its own fæces, etc. After the furious stage has lasted for two to three days palsy rapidly sets in, affecting first the muscles of the jaw, then those of the extremities, and finally the respiratory muscles, and so causing death from asphyxia. The total duration of the illness in the dog is usually from four to five days; it may, however, last ten days, and it may run its whole course in two.

The other clinical variety of rabies is "dumb" or "paralytic rabies." This is really similar to the terminal phenomena of furious rabies. Dumb rabies is more especially characteristic of the disease in the rabbit and rodents generally. It is, however, occasionally seen in dogs, and it is probable that it has occurred in man. In dumb rabies the sensory troubles are not marked. The dog is anxious and agitated, and this condition is rapidly followed by paralysis, affecting, it may be, the jaw, or causing paraplegia or hemiplegia, or even monoplegia. In dumb rabies the animal is necessarily unable to bite, and the disease is of far shorter duration, viz. two to three days. The urine frequently contains sugar, both in dumb rabies and in the later stages of furious rabies.

In man during the early stages the patient is anxious, fearful, depressed, often complains of thirst, and there is marked pallor. He is quite conscious and rational, and able to talk, although even at the early stages respiration is slightly interfered with, leading to interruption of his sentences; the restlessness and agitation increase, but the most striking phenomenon which the writer has seen in three cases of hydrophobia is the intense fearfulness of the patients and their extreme dread. Slight and intermittent delirium may be present and delusions may supervene, exceptionally the delirium passes into maniacal excitement. Thirst is a prominent symptom, but there is great difficulty in deglutition, especially of liquids, and any attempt to swallow causes violent spasmodic contraction of the muscles of deglutition, so that the fluid is often expelled from the mouth. Very soon the spasmodic contractions spread to other muscles, more especially those of respiration, and general convulsive attacks, with marked opisthotonos, supervene and recur at every attempt to swallow. These attacks rapidly exhaust the patient, the pulse becoming quick and irregular; the convulsive seizures increase in frequency, and death usually supervenes from asphyxia. The convulsive attacks are in the fully established disease produced not only by attempts at swallowing,

but also by slight reflex stimuli, such as a draught of air, or a strong light, etc. During the convulsive seizures the mental excitement of the patient is greatly increased. In very exceptional cases a condition similar to that of paralytic rabies has been seen in the human subject, namely, a rapid ascending palsy, affecting first the extremities, and then the muscles of respiration. It is possible that some of the cases described formerly under the term of Landry's paralysis may really have been cases of paralytic rabies. There is usually slight fever at the onset of the malady, and the temperature may rise to 105° F. Albumen and sugar may be present in the urine.

The statement that the patient barks like a dog has arisen from the fact that the accumulation of mucus in the throat, together with the partial palsy of the respiratory muscles, leads to a peculiar cough; and the frothing at the mouth sometimes described is due to the unswallowed saliva and mucus which hangs about the lips.

The duration of the disease in man is usually two to four days.

Morbid anatomy.—In animals the mucous membrane of the mouth, the tongue and larynx are congested and covered with an abundant dry mucus. The stomach, especially in the dog, contains no food, but a number of substances of the most diverse description; frequently there are petechial hæmorrhages in the mucous membrane and even hæmorrhagic ulcers; these may also be present in the intestines. The spinal bulb and brain are usually congested. Other lesions, such as petechial extravasations in the serous membranes, are perhaps more dependent on the mode of death than on the action of the virus of rabies. It is difficult to diagnose rabies from a post-mortem examination in animals, and is frequently impossible owing to the fact of the animal having been killed at an early stage of the disease before the lesions are fully developed, and it is for this reason that the experimental diagnosis by inoculation is of much value. The combination of the absence of food and the presence of a great variety of foreign bodies in the stomach is suggestive.

In man the main post-mortem features are the congestion of the fauces, larynx, trachea, stomach, and also of the central nervous system and meninges. Microscopically, hæmorrhages have been found by Gowers and others in the nerve centres, more especially in the fourth ventricle. Several observers have noted objective changes in the cells of the bulb and even the presence of collections of leucocytes, to which Gowers gave the name of "miliary abscess"

Diagnosis.—In diagnosing rabies, both in animals and in man, three methods are open to us—by the clinical characters, by the

post-mortem appearances, and by experimental inoculation. Clinically the most satisfactory method in animals is to isolate the suspected animal with due regard to the safety of others; if it be rabid, death will soon supervene with the characteristic paralytic symptoms, as the course of the disease is short after the establishment of the initial symptoms. On the other hand, if the suspected animal be killed, it may take several weeks to determine the existence of rabies by inoculation, and it is impossible to diagnose rabies on post-mortem examination in the early stages of the disease. The most common diseases in dogs mistaken for rabies are epilepsy, epileptiform seizures as a result of ear disease, and enteritis. The impaction of a foreign body in the throat often leads to a mistaken diagnosis of dumb rabies in animals.

In the human subject hystero-epilepsy, mania, tetanus, and Landry's paralysis are the maladies most apt to be confounded with hydrophobia. It is more difficult to separate mania than hystero-epilepsy from rabies, but such patients do not suffer from the characteristic respiratory spasm which is seen in hydrophobia. Tetanus which may follow the bite of a dog has a shorter incubation period and there is not that peculiar fearful expression that is so characteristic of rabies.

The term "lyssophobia" has been applied to a group of symptoms occurring in persons who are in great dread of rabies after having been bitten by an animal not necessarily rabid. A difficulty in swallowing, resembling the globus hystericus, together with hysterical convulsions, form the prominent symptoms. True spasm of respiration, such as is seen in rabies, is, however, absent. The real malady has more often been thought to be spurious than the converse.

After death the diagnosis of rabies can be made with certainty by inoculation of an emulsion of the medulla from the suspected case. It is possible, however, that putrefaction may in some cases prevent the detection of rabies even when present. The suspected medulla or spinal cord should be placed in glycerine for two or three days. An emulsion of it should then be made in sterilised salt solution or broth and a few drops injected subdurally in the rabbit. This plan is followed because it is the most certain method of communicating the disease, but inoculation into the aqueous humour is also efficacious. If the virus of rabies is present the rabbits develop paralytic rabies after an incubative period of from fourteen to nineteen days, sometimes, however, prolonged to six weeks. The characteristic features of this experimental rabies in the rabbit are a progressive paralysis occurring at the time when the general

nutrition of the animal is still good and accompanied with attacks of clonic spasm and dyspnœa. The mere occurrence of palsy of the extremities is not sufficient to diagnose rabies experimentally. The rabbits usually live for two or three days after the onset of palsy. The only fallacies in this method are, on the one hand, that exceptionally the presence of putrefaction in the suspected spinal cord has prevented the development of rabies owing to the destruction of the virus, and, secondly, that if the spinal cord is contaminated with some other virus, as for instance that of septicæmia, the inoculated animals may die before the incubation period of rabies has elapsed. This method of diagnosis is equally applicable to the spinal cord or medulla of man, and has been of use on several occasions in determining whether a patient has succumbed to mania or to rabies.

Treatment.—The part bitten should be washed as soon as possible, and temporary compression above the seat of the bite to delay and prevent absorption should be employed. The wound should then be thoroughly cauterised with strong nitric acid or with some strong antiseptic, such as carbolic acid. Nitrate of silver is not so efficacious as nitric acid and the latter should be used if possible.

The fully-established disease in man is beyond treatment, the only thing that can be done is to keep the patient absolutely quiet in a darkened room and to combat the violence of the spasms by chloroform or chloral. The Pasteur treatment is, however, of the greatest value in preventing the development of rabies both in animals and in man after exposure to the virus. It is essential that that treatment should be entered upon with as little delay as possible, and it is most unwise for the victim bitten by an animal to wait until the inoculation of rabbits with the suspected material has shown the animal to be rabid; in this way three weeks may be lost, and the disease may declare itself before the protective inoculations can be carried out. If, after a person has been bitten, the suspected animal be isolated, a delay of a very few days will determine whether there is or is not reasonable ground for looking upon the case as one of rabies, and the inoculation test can then be used to confirm this, but if there are good grounds for suspecting the animal to be rabid the Pasteur treatment of the person bitten should not be delayed for the results of the inoculation test. The essence of the Pasteur treatment is to inject subcutaneously an emulsion prepared from dessicated spinal cords of rabbits which have been inoculated with rabies. The potency of

the virus is gradually destroyed by dessication, and in this way by varying the period of dessication a series of emulsions of gradually increasing strengths can be prepared. The injection of these not only does not produce rabies but renders the animal or person immune to rabies at any rate for a time. The statistics of the Pasteur Institute not only show the great value of the treatment in preventing the onset of hydrophobia in those bitten by rabid animals, but they also show that the modern treatment as conducted there is free from risk.

JOHN ROSE BRADFORD.

FOOT AND MOUTH DISEASE

SYN. APHTHÆ EPIZOOTICÆ

An acute febrile affection, the most prominent feature of which is a vesicular eruption, occurring chiefly on the mucosa of the mouth, but also on the skin of the hands and feet, and sometimes on other parts of the body.

This epizootic malady, said to have been first imported into England in 1839, chiefly affects ruminants and pigs, but is transmissible to man. The contagium may be conveyed directly or indirectly, that is to say, it may be inoculated on a sore, or wound of the skin, or mucous membrane, or the infection may be derived from partaking of tainted milk, butter, or cheese.

Notwithstanding the severe and extensive outbreak among the cattle in the British Islands between 1876 and 1885, when the numbers attacked were counted by hundreds of thousands, and a further outbreak in 1892 of over 5000 cases, English medical literature relative to human infection seems confined to a few scattered cases, and an epidemic at Dover in 1884, where 144 persons were attacked. Therefore, either the disease, if it have occurred, has not been recognised as such, and has been assigned to some other cause, or the transmission of the infection to man is attended with some difficulty. On the continent of Europe, however, it seems to be fairly common, and there aphthous stomatitis in children is almost invariably assigned to infected milk and to a bovine origin.

The virus.—The actual exciting cause is still undecided, but claims have been raised on behalf of—a streptococcus (Klein, Kurth); a bacillus, pure cultures of which are stated to reproduce the disease (Starcovici); a protozoon, *Protamœba aphthogenes*, which has been detected in the vesicles and circumjacent tissue (Piana and Fiorentini). But whatever the virus may be it is certain that it is highly contagious to cattle, and may retain its infective power for quite three months.

The **incubation period** in cattle is stated to be a week, but in man it varies from two to eight days, the difference probably depending on the direct or indirect method of infection.

Symptoms.—The disease declares itself by a rigor, soon followed by pyrexia (101°-102°), malaise, and headache. The mouth feels hot and dry, and the feet and hands may burn and tingle. After lasting two to seven days the general symptoms are followed by an eruption of small vesicles on the mucosa of the mouth, any part of which may be affected, on the skin of the hands and feet, and sometimes on other parts of the body, notably the lips and face.

In the mouth the number of vesicles, except in bad cases, is rarely more than ten or twelve, and their distribution may be discrete or confluent. The vesicles are small yellowish-white blisters with turbid fluid contents, and may attain the size of hemp seeds or even of peas. After some hours to one or two days the vesicles burst, leaving shallow ulcers with red base and margins. The eruption in the mouth is accompanied by dysphagia, ptyalism, difficulty of speaking, and sometimes by offensive discharge from the nose. With the stomatitis are also associated pain in the mouth and swelling of the retro-maxillary glands. In severe cases symptoms of gastro-intestinal inflammation may be present, such as vomiting, diarrhœa, and occasionally sanious stools, symptoms which suggest that the alimentary mucosa may be in the condition of aphthous enteritis, as is the case in animals.

The stomatitis subsides gradually and the ulcerations heal in a week to a fortnight. The average duration of the disease is from two to three weeks, but it may be protracted to four weeks, or not last more than one.

The **prognosis** is extremely favourable, for nearly all the cases recover. But there are several instances where young children have succumbed to an attack.

There is no evidence to show whether one attack confers immunity.

The **diagnosis** should be comparatively easy if there be a vesicular eruption on the mouth, and on the hands and feet, especially in the inter-digital folds, occurring in a district infected with the epizootic. In large towns, however, and in cases where the eruption is limited to the mouth, the diagnosis becomes more speculative; but it should on no account be confused with aphthous stomatitis or with "thrush." The only disease with which this aphthæ epizooticæ is likely to be confounded is varicella. This might arise when the eruption in foot and mouth disease is scattered over the trunk and face. These cases are, however, rare, and the converse is more common; that is to say, the vesicular eruption is more frequently confined to the mouth.

The **treatment** of foot and mouth disease is simple. It is advisable to wash the mouth out frequently with mild solutions of chlorate of potash or of borax; to protect the eruption on the hands and feet from becoming contaminated with dirt, and dress them with lead lotion; and to feed the patient with a nutritious and liquid diet.

It would be advisable to boil the milk if there were an outbreak of foot and mouth disease in the district.

R. G. Hebb.

COINCIDENT OR MIXED INFECTIONS

It has for a long time been a common opinion that it is very rare, if not impossible, for more than one of the specific infectious diseases to simultaneously attack the same individual. This idea, for which John Hunter appears to have been very largely responsible, is still widely prevalent. But a search through the medical literature of the past century will reveal the error of his teaching, and its final refutation has been brought about within the last few years. The experience of any of the large fever hospitals furnishes ample evidence of the concurrence in the same subject of two or more infectious diseases. To illustrate this statement a reference to recent statistical reports published by the Metropolitan Asylums Board will suffice. Of 41,483 cases of infectious disease (chiefly scarlet fever, diphtheria, and enteric fever) admitted into the fever hospitals of London during 1896 and 1897, 1191 or 2.8 per cent

were at the time of admission suffering from more than one infection. By far the most common combination of diseases was that of scarlet fever and diphtheria, 589, or nearly half the cases. Frequent were scarlet fever and whooping-cough (186); scarlet fever and chicken-pox (163); diphtheria and measles (66); and scarlet fever and measles (65). Less common were diphtheria and whooping-cough (34); diphtheria and chicken-pox (27); and the combinations of scarlet fever or diphtheria with rubella or enteric fever, of which there were but a few instances. In addition to these cases, however, and usually in consequence of their having been unwittingly introduced during their incubation period to the general wards, there were those in which the patient contracted one infectious disease while convalescing from another. Thus, among 30,417 completed cases of scarlet fever—*i.e.* the cases discharged and fatal during the years in question—there were 1501 cases of diphtheria, 1018 of chicken-pox, 302 of measles, 197 of whooping-cough, and 168 of rubella. The number of diphtheria cases is large, doubtless because many are included in which the diagnosis was made on bacteriological evidence. Among 9789 completed cases of diphtheria there occurred 768 of scarlet fever, 100 of chicken-pox, 70 of measles, and 38 of whooping-cough; while among 1277 cases of enteric fever there were 9 each of scarlet fever and diphtheria.

The diseases to which the figures just given relate are those most prevalent in this country at the present day. But with them, as well as with one another, may be combined the following infections—smallpox, mumps, erysipelas, typhus fever, pyæmia, pneumonia, syphilis, tuberculosis, and malaria. There appears in fact to be no reason why any one specific infectious disease should not co-exist with any other. Usually two only are met with at the same time; but the writer has had under his observation several cases in which three or even four have attacked the same patient within a very limited period.

Inquiry into the relative frequency of concurrence shows that it depends considerably upon the etiology of the affections concerned. For instance, while it must be admitted that the figures given above afford only a rough estimate of the comparative frequency, yet it will be noticed that enteric fever does not often enter into these combinations. One of the reasons for this is that scarlet fever, diphtheria, measles, chicken-pox and whooping-cough are chiefly diseases of childhood, whereas enteric fever attacks individuals who have passed that period of life. Differences, therefore, of age-

incidence, of seasonal or annual prevalence, and of virulence, partly account for varying frequency of concurrence. But when allowance is made for these factors it still appears that diphtheria and scarlet fever have a great liking for one another, and that diphtheria is very ready to ally itself with several of the other specific diseases.

Another question of some interest is—Are patients, the subjects of one infectious disease, more likely, *ceteris paribus*, to contract another if exposed to its infection than healthy persons? Such facts as are forthcoming with respect to diphtheria occurring during convalescence from scarlet fever and *vice versâ* lead us to answer the question affirmatively, and it is certainly reasonable to suppose that a person weakened by one disease would less easily resist infection by another.

On one point clinical experience is quite clear; and that is, that when infectious diseases occur together, or quickly follow one another in the same patient, the symptoms are, as a rule, more serious than when they occur alone. The fatality of diphtheria co-existing with or immediately following scarlet fever, measles, or whooping-cough, is much higher than when it occurs singly, as also is that of measles following scarlet fever; and so on. If measles or scarlet fever attack a person already the subject of any tuberculous lesion, not only is the latter apt to be aggravated, but complications due to the former diseases are the more likely to arise. Beyond, however, this intensification of severity, concurrent infectious diseases do not appear to influence one another's course. From all that has been said, it is quite clear that one infectious disorder does not protect against another, a fact which may be used as an argument in favour of the opinion that vaccinia is essentially the same as smallpox. If not, then the antagonism of vaccinia and smallpox forms a striking exception to the general rule.

So far we have dealt with diseases of which the symptoms are well defined, and whose distinct entity has been known for long periods, in some instances for centuries. But bacteriology has shown us that certain forms of disease, hitherto included under such general terms as pyæmia and septicæmia, are due to the action of certain pathogenic micro-organisms; and it has further demonstrated that many of the morbid processes associated with diseases, whether specific or not, are due to the secondary invasion of the tissues or fluids of the body by these micro-organisms. As an example, we may refer to measles. One of the most common

and fatal complications of this disease is broncho-pneumonia. There is good evidence, both bacteriological and clinical, to show that this affection is not due to the essential cause of measles. The infective agent of measles appears to set up catarrh of the respiratory tract, and thus to weaken its resistance to the action of such organisms as the pneumococcus and certain strepto- and staphylo-cocci. In a case of measles, therefore, complicated with broncho-pneumonia, we have an example of a mixed infection. Some of the complicated cases of scarlet fever, enteric fever, and diphtheria, furnish us with similar illustrations. Probably further investigation will prove this principle to be of very wide application. There is reason to believe that the various organisms of which we have been speaking may lead a saprophytic existence, and that it is only under certain circumstances that they become pathogenetic. This is true of so specific and malignant an organism as the diphtheria bacillus. It may, therefore, be suggested that these organisms have their seasonal variations of prevalence and virulence in much the same way as do such primary infections as smallpox, scarlet fever, and diphtheria; and that the difference in type of the latter (primary) is due largely to the variations in type of the former (secondary) infections.

The concurrence of two or more infectious diseases in the same patient is a frequent source of difficulty in diagnosis. It would, in fact, be quite impossible to detect some combinations, such as rubella co-existing with measles. But a careful attention to the individual symptoms of each separate disease will often assist the avoidance of error.

The only point worthy of mention here with respect to treatment is the necessity of providing in hospitals for infectious diseases a sufficient number of separate rooms or wards for the isolation of such cases of mixed or coincident infections as are sure to occur.

E. W. Goodall.

DYSENTERY

Although the word "dysentery" serves to designate a disease possessing fairly well-defined clinical and anatomical characteristics, it is possible, nay probable, that several ailments which ought to rank separately are associated under the term. Of these, dysentery ascribed to hepatic derangement, to malarial infection, to scorbutus, to bad food, impure water, or other sanitary defect, to the presence of the amœba coli, and to other micro-organisms in the intestines, are a few of the varieties commonly enumerated. The catarrhal form of the disease met with in colder climates, and the dysentery met with in the tropics in an endemic form, illustrate further the wide divergence of types which obtain. Of these, however, the only variety which approaches scientific precision is the so-called "amœbic dysentery." That the amœba coli is met with frequently, but by no means invariably, in dysenteric stools is undoubted; that it is met with in every case during certain epidemics may be also true, and yet its presence may in no sense bear the pathological significance claimed for it by many writers. With this equivocal exception, therefore, no scientific division of the group of diseases, believed to be covered by the name "dysentery," as determined by their parasitology, etiology, or pathology, has been as yet arrived at.

Acute dysentery is characterised by an intestinal flux, consisting, at the commencement of the illness, of loose fœculent matter mixed with blood and mucus. The fœculence speedily disappears, and the stools present a flocculent, slimy, jelly-like substance, mixed with blood. In aggravated forms of the disease the mucous and submucous coats of the intestine undergo necrosis, when the evacuation yields a putrid odour and contains gangrenous sloughs floating in a thin, brownish, blood-tinged liquid. The flux is accompanied by febrile disturbance, by acute abdominal pains, by tenesmus, and by nervous and physical prostration. Dysentery may end in resolution and complete recovery, in permanent damage to the gut (chronic dysentery), in causing liver abscess, in gradually advancing asthenia, or in death so speedy that the term "malignant" is applied to it.

Etiology.—That several varieties of dysentery possess a specific cause is the present-day belief, although little or no direct evidence can be said to justify the conclusion; *malaria* is held to be a cause

of dysentery, because dysentery prevails endemically in malarial countries, because the febrile disturbance accompanying the disease resembles malarial fever, but more directly still because some cases of dysentery are "cured" by quinine. The frequent association of malarial infection with dysentery must never be lost sight of; many hold the opinion that malaria is the principal determining factor in the etiology of the disease, and it is well-nigh imperative, before proceeding to treat a case of dysentery, that the blood be carefully examined for malarial parasites. Malaria, whether as a cause, a complication, or a sequela, is so intimately associated with dysentery that quinine must not be altogether neglected in the treatment of the disease.

Scurvy, if not an etiological factor, is not unfrequently a concomitant ailment in dysentery. In simple scurvy the bowels are usually constipated, but as lowering of the vitality is apt, under certain conditions, to invite a scorbutic condition, so in dysentery of some standing, when the patient is unable to consume anti-scorbutic nourishment, scurvy may supervene. The appearance of the symptoms of scurvy in the course of an attack of dysentery will determine the line of treatment to be adopted.

In climates such as the Soudan, in which there is a marked difference between the night and day temperatures, *chill* is a potent factor in causing dysentery. During a military campaign, be it in India, Southern Europe, or the United States, when the troops are insufficiently protected from the cold of the night, dysentery develops with a rapidity and certainty which can only be put down as cause and effect. Whether it is the liver and consequently the portal circulation which is primarily affected by the cold, or whether it is the direct action of cold on the intestines themselves, is not known; possibly both viscera directly suffer.

Dysentery is also enumerated as one of the water-borne diseases, and certainly in those towns in which an improved water-supply has been obtained, dysentery has abated in virulence, and in the extent of its prevalence. On board ship confirmatory evidence as to the pollution of the water-supply being a direct cause of dysentery is plentiful. The possibility of direct infection by the use of a common latrine must not be lost sight of, whether the virus is considered to enter by the anus, the mouth, or the nostrils. Any condition which tends to lower the strength or derange the health of the individual during the prevalence of dysentery, especially in an epidemic form, is calculated to reduce the powers of resisting the toxic agency of the disease.

Parasitology.—In 1875 Losch described a protoplasmic parasite, the *amœba coli*, as occurring in the stools of dysenterics in Russia, and since then the amœba has been found by observers in many countries. The writer met with the amœba in nine consecutive cases of dysentery in Hong-Kong; in three cases of malignant dysentery, however, he failed to find it; and others record a similar experience. When a small fleck of the flocculent mucus of a dysenteric stool is placed on a warm (100° F.) microscope stage, immediately after being passed, the presence of the amœba coli may be recognised. Its large size (6 to 35 μ), its mobility, its pale-greenish colour, and its strongly refractive powers, arrest the attention. The mobility is in most cases, though not in all, very marked. Pseudopodia are extruded from the circumference, and then withdrawn to again appear at another part of the mass. The amœba is not only altered in shape by the pseudopodia, but the mass changes its place, travelling either towards the point of least resistance, or in the direction of alimentation. Cold (75° F.) and heat (110° F.) arrest the movements which, under favourable circumstances, might continue for a couple of hours or more. At rest, the body of the amœba coli is seen to consist of a thin, pale-greenish, outer covering or ectoplasm, and an inner, granular, darker endoplasm. A nucleus is present, and in stained specimens a nucleolus. The amœba may engulf red corpuscles, micrococci, bacilli, and more rarely leucocytes and pigment. Vacuoles are a fairly constant phenomenon. The arguments for and against the amœba coli being the cause of dysentery are—(1) That many observers have found it in scores, in one case in hundreds, of well-nigh consecutive cases. (2) That the injection of material containing active amœbæ into the rectum of several varieties of animals has been productive of dysenteric symptoms. (3) The amœba coli, however, is met with in health, with or without the exhibition of a severe purge, and it is possibly a constant occupant of the cæcum and upper part of the large intestine.

Dysentery has also been ascribed to other micro-organisms, some of them normal inhabitants of the intestines, such as the bacterium coli commune, which is accredited by some with taking on special pathological properties. Others refer dysentery and liver abscess to streptococci, and on quite inconclusive grounds other toxin-producing micro-organisms have been regarded as the cause of the disease.

The difficulty of framing an accurate definition of dysentery, or a satisfactory conception of its pathology, due to the uncertainty

both as regards the nature of the specific cause of the disease and of the real value to be attributed to the several conditions which experience shows are so frequently associated with its occurrence, is further complicated by the variety in its clinical course and features which is to be observed in various epidemics and in different localities. "These and other circumstances seem to point to radical differences in the several forms—differences of cause as well as differences of symptoms, course, and sequelæ. It is well, therefore, to regard the term 'dysentery' as but the name of a symptom, or group of symptoms, indicating an inflamed condition of the colon, and not as indicating a single and well-defined disease. Dysentery simply means inflammation of the colon. There may be many kinds of inflammation of the colon" (Manson).

Geographical distribution.—Leaving the epidemic dysenteries of colder climates out of the question, dysentery increases in frequency as the Equator is approached. Dysentery is endemic in many tropical localities, but may spread thence in an epidemic form to adjacent countries. It may be safely stated that in those countries in which a real improvement in sanitation has taken place, dysentery has well-nigh disappeared.

Symptoms.—A typical case of **acute dysentery**, as met with in practice in the tropics, is characterised by the following signs and symptoms:—During what appears to be a simple intestinal catarrh, or commencing suddenly, shreds of mucus appear in the evacuations; the stools become more frequent, and are attended by some sweating and a feeling of abdominal weakness after being passed. Blood tinges the mucus, or is in sufficient quantity to stain the whole fluid of the stool. Gripings (tormina), tenesmus, and an increasing desire to pass a motion supervene, and the patient's calls for the bed-pan become almost incessant. All trace of fœculence disappears, and at an evacuation a tablespoonful of blood-stained, foul-smelling, jelly-like material, attended by great straining, may be all that is passed. The tongue becomes coated and furred, the mouth is clammy, the saliva tenacious, a feeling of nausea frequently occurs during the early stools, but vomiting is rare. The abdomen is tender, especially over the lower part of the colon in the left iliac fossa, the anus is excoriated, hot and burning, and the bowel may be prolapsed. Movement causes palpitation, and the pulse becomes small and frequent. Urine is scanty, high coloured, and occasionally suppressed; strangury and retention are also possible complications. Increase in temperature is constant, but, except in the malignant form, the thermometer seldom

registers more than 101° or 102°. In the acute form dysentery may continue several days, or in young strong men for as many as twenty or more days, and yet the patient may make a good and permanent recovery. Frequently, however, if signs of abatement do not appear towards the end of the first week or earlier, the disease assumes a type which betokens danger to life. The stools may contain shreds and sloughs floating in a fluid of dark-brown hue and smelling abominably. The tongue looks red and glazed, or is coated by a brown fur; sordes cover the teeth, the abdomen becomes tympanitic and tender, and hæmorrhage may occur from the bowel, or from the mouth and nose. The temperature rises to, and continues at, 104° or higher; the pulse at the wrist is small, feeble, extremely rapid, and frequently irregular. Hiccough may become persistent, and the patient, after passing through a low, nervous state, during which all painful sensations abate or cease, dies in a state of coma.

The disease may end in one of three ways:—In convalesence and complete recovery; in chronic dysentery, with permanent damage to the intestinal wall; or in death from collapse, from hæmorrhage, from peritonitis caused occasionally by perforation, from exhaustion, or after passing through a typhoid state. Sudden death, attributed to heart failure, may occur during convalescence, even when the stools are assuming a natural consistence.

Varieties.—Acute dysentery receives a variety of names according to the assumed cause, and the signs and symptoms that predominate. Most of these names, coined from mere clinical variations, are counterfeit, and but add to the chaos of nomenclature. *Malarial* dysentery presents few specific clinical phenomena. Apart from the history, the presence of the malarial parasite in the blood, and the variations in the temperature of the body, the most marked symptoms are a tendency to early prostration and algidity, and the loss of a large quantity of blood by the bowel. The curative effect of quinine, however, has done most to stamp this variety of dysentery as malarial. The so-called *purulent*, *gangrenous*, and *fibrinous* or *pseudo-diphtheritic* varieties are all preceded by, and are but the natural sequelæ of an unchecked, simple, or catarrhal dysentery. The continuance of the specific irritation of the bowel may lead to the infiltration of its walls with fibrinous material or with pus, to the formation of ulcers, and, when the infection is still more virulent, to obstruction of the blood vessels and sloughing of the mucous and submucous coats of the bowel. When the wall becomes extensively infiltrated with a fibrinous deposit, the gut

becomes somewhat rigid, the calibre variable, wide in parts and narrow in others, and an incision into its tissue betrays a rather tough semi-cartilaginous consistence. The names *scorbutic* dysentery and *typhoidal* dysentery indicate either the association of an intestinal flux resembling dysentery occurring during an attack of scurvy, typhus, or typhoid, or, that a dysenteric attack assumes, during its course, features peculiar to either scurvy, typhus, or typhoid. *Hepatic* dysentery is a convenient term whereby the early implication of the liver in the dysenteric attack is prominently noted. On the one hand the condition of the liver may be a primary etiological factor or, on the other hand, the liver may be infected during the course of the disease in the bowel by way of the portal vein. When vomiting is prevalent, the liver enlarged and tender, and considerable pain in the right hypochondrium supervenes during an attack of dysentery, it is usual to stamp the variety as hepatic. The *dysentery of war and famine* occurs independently of climate and season; it is an extremely fatal form, and there seems little doubt it is contagious. So-called *amœbic* dysentery is stated to exhibit marked chronicity, frequent relapses, and a pronounced tendency to cause liver abscess. In the stools the amœba coli is necessarily present, but none of the signs or symptoms are sufficiently constant to define the amœbic form as a specific clinical variety.

Chronic dysentery.—The acute form of the disease frequently results in a chronic dysentery. After the acute symptoms have subsided, and stools possessing fœculence and some consistency are passed, instead of complete recovery following, the mucous flux may persist, pain of a subacute character remains, and the general health of the patient does not improve satisfactorily. As time passes the stools may become fairly well formed or constipated, and yet jelly-like or muco-purulent matter, and occasionally blood, accompany them. This fluid material, as a rule, precedes the stool, showing that the seat of the trouble is just within the anus. Hæmorrhoids, and painful ulcer of the rectum, are frequently associated with or mistaken for dysentery, and it is at times difficult to ascertain the origin of the trouble. Pressure in the left iliac fossa over the sigmoid flexure, and sometimes in the right iliac fossa over the cæcum, elicits pain; and the sigmoid flexure may be felt to be indurated, enlarged, and tender. The stools are irregular as to the time of their being passed as well as in the character of their consistence. Exposure, fatigue, and inadvertence in diet may induce a semi-acute attack, causing an aggravation of the diseased state. This may continue until a chronic state is established, the

bowel being so altered that the ulcerated surfaces become incapable of healing, or, should they do so, pronounced cicatrices and narrowing of the gut ensue. In chronic dysentery the tongue may become red, raw, and fissured, the appetite at times may be voracious, and at others in abeyance; the stools retain some of their disagreeable odour, and in some cases are of unusual bulk, and seemingly fermenting. The patient's health suffers; he becomes sallow, emaciated, cachectic, and in the gravest cases hectic appears, attended by anæmia and sweatings; a fatal issue is then at hand, and death results either from gradual exhaustion, or from some concomitant ailment, with dropsy, pneumonia, or cardiac failure.

Dysentery and liver abscess.—The relation between dysentery and liver abscess is an important one clinically and pathologically. Many observers believe that in almost all, if not in all, cases of liver abscess, a previous history of dysentery can be elicited; whilst, on the other hand, a few attempt to disassociate the ailments. Analogy, however, favours the conclusion that the two are associated, as in most ulcerative and inflammatory lesions of the intestine, other than dysenteric, there is a marked tendency to the deposit of infective and purulent matter in the liver substance. Clinical experience shows that liver abscesses were found by Woodward in 21 per cent of autopsies on patients dying of dysentery; and in as many as 60 per cent of cases of liver abscess a history of dysentery was elicited by Kartulis in Egypt. Many circumstances, however, pronounce against the conclusion that dysentery is an invariable antecedent of abscess. None more so perhaps than the fact that although dysentery is very prevalent amongst natives, abscess of the liver is rarely met with. The whole question, however, turns upon the question whether there are not several varieties of liver abscess. In the majority of intra-hepatic abscesses no doubt dysentery is the primary factor, but in those abscesses which form not *in*, but *upon* the liver, and most frequently between the layers of the broad ligament of the liver, it is difficult to explain a positive connection. Although the presence of the amœba coli in the intestines and in liver pus would seem to point to a relationship of cause and effect, it must be noted that the parasite is not usually found in pus issuing from a liver abscess until the third or fourth day after the abscess has been opened or tapped. Not only so, but liver pus is peculiar in that it is frequently "sterile" when first drawn off, none of the usual purulent organisms being demonstrable.

In a paper read at the annual meeting of the British Medical Association, 1899 (*Brit. Med. Journ.* 9th Sept. 1899), the writer

divided liver abscesses into two varieties, suprahepatic and intrahepatic. The latter is the result of dysentery; the pus shows the usual purulent organisms, streptococci, etc., and the amœba coli is perhaps present from the first. The suprahepatic abscess is non-dysenteric in origin, the pus is sterile and the amœba coli does not appear in the pus until after the third day of drainage. The pus from an intrahepatic abscess tends to reach the surface by way of the abdominal wall, but may burst into the peritoneum, the stomach or duodenum, the ilio-lumbar region, the bile duct, the vena cava, or even into the kidney. Suprahepatic pus tends towards the thorax, and, pointing upwards through the diaphragm, may reach a bronchus, when it is expectorated or may find its way into the cavity of the pleura or pericardium.

Post-mortem appearances.—In the simple forms of acute dysentery, although the opportunities of study are necessarily limited, the conditions are primarily similar to those met with in acute colitis and enteritis. In rapidly fatal cases of the gangrenous or malignant type, however, the lesions are unfortunately more frequently seen. The changes in the bowel in the latter form are destruction of extensive areas of the mucous and submucous coats of the large and occasionally of the small intestine; ulcers of all sizes with undermined edges, and frequently with sinuses communicating between neighbouring ulcers, exist in large numbers. The ulcers in the wall of the gut frequently coalesce, and a ragged, uneven, patchy surface may extend the entire length of the colon. In the swollen mucosa small abscesses, varying in size from a pin's head to a pea, stud the tissue. When cut into they are seen to be closed sacs containing a tenacious pus, but the apices of others may be found open, emitting pus when squeezed, and it is possible, nay probable, that the formation and bursting of these abscesses is but the initial stage of the ulcerative process. What remains of the inner coats of the intestine appears swollen, raised and injected, or here pale and there red and congested. The floors of the ulcers present an ashen-gray colour, where the sloughs have been detached, or the muscular coat may even be exposed to view. The lesion is usually most marked in the rectum, sigmoid flexure, and descending colon, but the disease may involve the whole of the large gut, the cæcum becoming the seat of advanced ulceration and sloughing. The disease may also spread through the ileo-cæcal valve and involve the small intestine to the extent of a foot or two. Although in dysentery the gut is so deeply ulcerated that a mere transparent film of tissue remains, perforation is rare. Frequently a protective

local peritonitis bars the way to extravasation of the intestinal contents. Everything points to the rectum being the primary seat of the disease; so markedly is this the case, that it would seem in fact as though the infective process started from the anus, and several observers are of this belief. Many believe that defecation over a freshly passed dysenteric or choleraic stool is a source of direct infection by way of the bowel in these respective diseases, and there seems some evidence in favour of the assumption.

In chronic dysentery the gut presents very diverse conditions. The colour of the mucous surface becomes for the most part much darker, and in parts brownish black. Old irregular cicatrices of healed ulcers are everywhere met with between the elevated, thickened, and indurated mucous ridges. The whole wall of the bowel is in parts hypertrophied and the lumen narrowed, in parts thinned and atrophied, as if a mere touch would cause rupture. Recent abscesses may be present, and sinuses may be found passing beneath bridges of cicatricial bands and constrictions. The mucous and glandular structures are never reproduced when once destroyed. In consequence of these conditions, dilatations and contractions of the calibre of the intestine are frequently seen.

The liver in acute dysentery is congested and enlarged, and with single or multiple intrahepatic abscesses. In chronic dysentery the liver is more frequently met with of reduced size; but owing to subacute attacks of dysentery supervening, the liver may be deeply congested, or become the seat of abscess.

The spleen varies in size and consistence; in acute dysentery it is usually full, soft, and deeply congested, whereas in the chronic form of the disease it is either considerably and permanently enlarged or markedly diminished in bulk.

Towards the end of a fatal case, the lungs and kidneys may become involved, but these viscera are not primarily affected during dysentery.

Diagnosis.—The signs and symptoms stamp dysentery, in the sense of a dysenteric flux, decisively; but the variety of the disease under treatment may be difficult to decide upon. It is frequently by a process of exclusion during the progress of a case that one decides whether the dysentery is of the hepatic, the amœbic, the scorbutic or of the malarial variety, and this information may be gathered solely by the effects of treatment upon the disease. Chronic dysentery is diagnosed chiefly by the history of the case, but in part also by the nature of the stools. Several affections may set up a condition allied in symptoms to dysentery. A fibrous stricture of

the rectum, malignant or syphilitic, especially in old tropical residents, may either mask, or be masked by, dysentery. Proctitis, painful ulcer of the rectum, the diarrhœa of Sprue, or in fact any intestinal flux may complicate, or be mistaken for chronic dysentery. In certain tropical countries the presence of the round worm or of other intestinal parasites may produce a fœcal irregularity which may lead to mistakes in diagnosis and consequent errors in treatment.

Although, however, the term dysentery is regarded as a convenient name for, it may be, a number of ailments arising from independent causes, there are a number of signs and symptoms which determine its presence; of these the chief are: general abdominal tenderness, tormina immediately before, and tenesmus during and after a motion; the stools consist of mucoid material tinged with blood, but if the disease persists, they contain a bloody slime, gelatinoid particles, and, in advanced cases, gangrenous sloughs smelling abominably. An increase in temperature, intense thirst, a furred tongue and rapid loss of strength serve, with the above abdominal symptoms, to stamp the disease as dysenteric. Ulcerative colitis is the name assigned to a condition of the bowel which, in pathological and in many clinical features, resembles dysentery. Colitis, however, occurs in temperate climates and in persons who have never visited the tropics; moreover, the tenesmus, the burning pain at the anus, the unceasing desire to go to stool, etc., so harassing in dysentery are not met with in ulcerative colitis.

In all cases of doubtful nature, a digital and specular examination of the rectum ought to be made.

Prognosis.—When the malignant characters set in early in the disease, there is but little hope of saving the patient; and when a chronic dysentery continues for a year or two, there is little chance of a permanent cure. Simple acute dysentery, however, is not in itself a fatal disease, the only sequela likely to happen being a chronic dysentery of some duration; at any moment, however, a simple case may assume a malignant type.

Mortality. — The death-rate in dysentery varies with race, environment, and type of the disease. Natives succumb more readily than Europeans in the tropics; the former show a case mortality of from 37 to 40 per cent, whilst the latter, according to Indian statistics, show one of from 3 to 22 per cent. Environment plays an important part in the chances of recovery. A European enjoying good sanitary surroundings, good food, and scientific treatment stands a much better chance of recovery than the native in

his squalid abode, with his crude medicines and indifferent food. The type of the disease, however, largely determines the mortality, malignant dysentery allowing but a small chance of recovery, for it must be considered one of the most fatal ailments known. The danger of an attack of dysentery, however, is by no means over when the acute symptoms have subsided; chronic intestinal troubles are apt to be set up, leading to contraction and obstruction of the intestine, loss of power of assimilation and consequent wasting, chronic diarrhœa, and greater vulnerability to attacks of intercurrent diseases.

Treatment.—The principles of treatment of *acute* dysentery are rest, suitable diet, and either arrest of the intestinal flux by appropriate remedies or its elimination by purgatives. The rest should be absolute; the patient should be confined to bed, and the use of the bed-pan insisted upon. The writer, however, goes further than merely obtaining general rest, and recommends the application of a large, thick, firm pad, big enough to cover the whole front of the abdomen; retaining the pad by a broad, tightly applied binder round the body. Alternately applied wet and dry pads, or a continuously applied wet pad increases the effectiveness of this device. Rest may be further procured by morphia hypodermically, or by opium given by the mouth or rectum; the plan of giving castor oil ʒiij, with 20 minims tincture of opium, in the very early stages of dysentery, has everything to recommend it. At the onset of an acute attack food should be reduced to a minimum. Rice-tea (rice, browned in the oven and infused with boiling water), or whey are to be given in sips, and ice pellets may be sucked if the thirst is intense. Ordinary weak tea, without milk or sugar, is a very grateful beverage in dysentery.

When dysentery proves intractable to these simple remedies, ipecacuanha should be given. The formula for administration is as follows:—Two hours before the time selected to give the drug all food is to be withheld, and only small pieces of ice given to suck. Twenty minutes before giving the ipecacuanha, half a grain of morphia may be administered hypodermically, or 25 minims of laudanum is to be exhibited by the mouth. Ten minutes before the ipecacuanha is given, place a mustard leaf, or mustard plaster the size of the hand, on the epigastrium. Give 30 grains of ipecacuanha root freshly prepared, in pills, cachets, or wafer paper. Five or ten minutes after the administration, remove the mustard plaster. Insist upon the patient keeping quiet with the head low, and give particles of ice to suck. No other food or drink is allowed until

at least three hours afterwards, when sips of weak tea or rice-tea will be found to be most beneficial. The continuance of the ipecacuanha treatment will depend upon the character of the stool. One dose may bring down a fœculant stool, but, failing improvement, the drug may be continued twice a day in 10-grain doses for several consecutive days.

Malaria may be either a cause or a complication of dysentery, and, should ipecacuanha fail, quinine is indicated in, say, 5-grain doses every six hours for two days. In pregnant women both ipecacuanha and quinine may be given if opium is freely administered at the same time. Scorbutus is not unfrequently the genesis of dysentery, and the reputation gained by several "native" remedies arises no doubt from their efficacy in this variety of the disease. The fresh plants, leaves, or fruit supply the vegetable acids required for the treatment of scurvy in whatever form it may appear. *Simaruba* bark is much in vogue in the southern countries of North America. It is exhibited in a variety of ways; the best, perhaps, is in the form of infusion obtained by boiling 1 oz. of the powdered bark in 3 pints of water until the quantity is reduced to half the bulk. One-half the quantity may be given morning and evening. The writer has experience of *mangostine rind* in the treatment of dysentery; and in the Straits Settlements and throughout Malaya it is held in high esteem. It is best prepared by boiling the rinds of three dried mangostines in 1½ pint of water until the quantity is reduced to 1 pint. One-third of the pint is given thrice daily. The *Monsonia ovata* is a South African plant from which a tincture (1 in 8, alcohol, 90 per cent) is made and administered in doses of 1 to 4 drachms every four hours. In India *bael fruit* is extensively used. The preparation must, however, be made from the fresh fruit, so that its efficacy can, like many other native remedies, be only ensured locally.

The aperient treatment may be tried when ipecacuanha, quinine, etc., fail, or it may be employed from the onset. There are two methods of administration: (*a*) ½ oz. of the sulphate of sodium or magnesium dissolved in a small quantity of hot water may be given to commence with, followed by smaller doses every six or eight hours; (*b*) or 60 grains of either of these salts may be given every quarter of an hour or every half hour until the stools show signs of fœculence. When drugs fail, the writer places most reliance on an ample cold (ice cold if necessary) wet pack applied to the whole front of the abdomen. Pressure is maintained by a bath towel wrapped tightly round the body from mammæ to groins.

Re-apply the wet pack every two hours, and persevere with the treatment for thirty-six or forty-eight hours. In many cases this plan of treatment well deserves the title "specific." The treatment by calomel and opium is worthy of trial when other means fail, either with, or without, ipecacuanha. These are given in combination, in doses of 1 grain of each every six hours.

Although the stools become fœculent, they may remain quite loose, and this diarrhœa may require to be arrested by some one of the many astringents in use; bismuth and opium usually suffice, but sulphate of copper, of zinc, or of iron, are also employed for the purpose.

Attempts at disinfection of the bowel by such substances as salol in gr. 20 doses, by creolin (gr. 3), by napthalin (gr. 5), by tar (gr. 5), by creasote (min. 20), and a host of other drugs have been employed, and with but ephemeral success. Injections also of disinfectants by the bowel can only be of evanescent value, as to keep the intestine "sweet" a constant stream of the injection would have to be kept up.

In malignant dysentery, when sloughs are being passed and the patient's strength is becoming rapidly exhausted, "specific" drugs are well-nigh useless. Instead, every form of rational stimulant must be employed to, if possible, tide the patient over the stage of acute depression. In this variety the use of disinfectants for the intestine is theoretically sound, but practically the plan is not of much value owing to the difficulty of its application.

When dysentery becomes *chronic*, the use of drugs is disappointing. Ipecacuanha loses its power, and it would seem as though the ragged, ulcerated, and congested gut demanded local treatment. A copious enema of plain boiled water (allowed to cool to 100° F.), followed, when the water has been passed, by an injection of 1 or 2 pints of boracic acid (saturated solution) or nitrate of silver ($\frac{1}{4}$, $\frac{1}{2}$, or 1 grain to the ounce of warm distilled water) are efficient remedies. The injection ought not to be forcibly given by an enema syringe, but by an india-rubber tube and a funnel held not more than two feet above the level of the patient's body as he lies in bed. The astringent injection should be retained for an hour if possible. After many trials of the long tube for the bowel, the writer has discarded it as unnecessary and dangerous. The injected fluid finds its way along the gut, if introduced slowly, more readily by syphonage than when administered by either an enema syringe or by a long tube.

Of the many drugs and methods employed in the treatment of

chronic dysentery, the writer relies on rest in bed; cold wet packs twice a day, morning and evening, for two hours; an occasional dose of castor oil; subnitrate of bismuth in gr. 20 doses, given in combination with 1 drachm of the confection of black pepper, and washing out the intestine by astringent lotions. In the constipation which so frequently follows dysentery, cascara in moderate doses, administered daily for a month or two, is an effective remedy.

Diet.—A purely milk diet is the usual routine of treatment in intestinal flux, whatever is the cause. The milk is given in sips, or in very small quantities repeated frequently. Some prefer the milk warmed, others exhibit it with ice. In the acute initial stages of the disease, however, milk does not seem suitable, and in its stead rice-tea, weak chicken broth, whey, ordinary very weak tea (cold or warm), barley water, or koumiss may be given. In chronic dysentery the writer finds the treatment by meat and "meaty substances" the most efficacious. The patient is fed thrice daily on beef, reduced to a fine mince, which, after being very lightly cooked, is served up 5 oz. at a time. Nothing but salt, and maybe the white of an egg, is given with the meal. Between meals and during the night the patient is allowed to eat calves' foot jelly freely. Hot water is the best drink, taken a quarter of an hour before or half an hour after meals. If the patient is too weak to take beef in this form, he may be fed on teaspoonfuls of freshly-made raw meat juice every ten minutes; scraped raw beef, and raw meat sandwiches being added as the strength gains, and the intervals lengthened as the power of digestion improves. A change to a temperate climate is an essential element in the treatment of Europeans suffering from dysentery when the disease threatens to become chronic. When hepatic derangements are concomitant, a course of treatment at a medicinal spa, more especially that of Carlsbad, is highly to be recommended.

James Cantlie.

MALARIA AND MALARIAL FEVERS

A group of specific diseases, characterised by fever of an intermittent, continued, or remittent type, giving rise to anæmia, with pigmentary deposits, and tissue changes in the spleen, liver, and other organs. The parasites occupy and destroy the red blood corpuscles. Certain species of mosquitoes and possibly other blood-sucking insects serve as intermediate hosts in the life cycle of the parasites.

Distribution.—While yet Western Europe and the Mediterranean littoral were the only countries known to civilisation, malarial diseases were almost universally distributed within them. In England, and even in Scotland, malaria at one time prevailed, but with better drainage, reclamation of swampy lands and improved sanitation generally, malaria has receded from its more northerly sphere.

When other continents became known to European travellers and colonists, it was found that no country north of the Equator from the Arctic circle to the Tropics was free from malaria; but as the Tropics were approached, however, it was found that malarial disease became more prevalent. In North America also malaria is gradually receding before drainage and cultivation, until at the present time it is seldom met with north of the 45th degree of latitude. Countries to the south of the equatorial belt are less malarial than similar latitudes to the north, and in those south of the 30th degree of latitude malaria is all but unknown.

Etiology.—Although not the only factors in determining the prevalence of malarial fevers, there is no doubt that a marshy soil and a high mean temperature are favouring agents. The delta of a great river, and low-lying land possessed of a high subsoil humidity, as at the foot of a mountain range, are the special habitats of paludism. Freshly-broken soil, especially virgin soil, is often intimately connected with outbreaks of malaria.

In all warm climates particular seasons of the year are associated with special liability to fever, and to the different seasons fevers possessing different types are ascribed. So pronouncedly is this the case, that such names as "spring and early summer intermittents" and "æstivo-autumnal" are used to divide one class from the other, which, as their names indicate, prevail during the spring and autumn respectively. The "unacclimatised" European seems more

predisposed to attacks of malarial fever than the coloured races native to hot countries. Children and young adults are specially liable to malarial infection, but old people of long residence in tropical countries are by no means immune. Females are not less prone to malaria than males, but they are usually less exposed to its influence.

The malarial parasites.—It was not until the year 1880, when Laveran discovered the parasites in the blood of persons suffering from malarial fever, that we had any scientific knowledge of the etiology of malaria.

The organism is termed, usually, the "plasmodium malariæ." The name is biologically incorrect, as the parasite is in no sense the large multinuclear mass of protoplasm which the designation would indicate. Zoologically, the malarial parasite is referred to the Protozoa, grade Corticata, class Sporozoa; and of the Sporozoans it most nearly resembles the Coccidia.

Examination of the blood for the plasmodium malariæ.—Wash the tip of a finger with soap and water; dry the part and then wipe it with ether or alcohol. Tie a cord round the root of the finger and prick the pulp with a sterilised needle. Wipe away the first drop of blood that issues, and with a clean cover-glass lightly touch the issuing blood so that a minute quantity adheres to its under surface. Place the cover-glass so charged on a clean slide without pressure and examine by $\frac{1}{12}$th inch oil-immersion lens. A number of such specimens may be mounted in a similar manner, and to prevent evaporation it is well to "ring" the cover-glass with vaseline. Freshly-drawn blood so prepared may be used for several hours for purposes of examination.

To stain the malarial parasite.—Instead of using a cover-glass to receive the blood, Manson recommends that a piece of thin paper be made to touch the drop of blood as it issues from the finger. The paper so charged is then drawn along the surface of the slide so that the blood is smeared on the glass in a thin layer. When the blood stain is dry, absolute alcohol is dropped upon its surface and allowed to remain for five minutes, when the alcohol is run off and the specimen again dried. To the blood thus fixed a staining fluid of one or other of the following substances is added:—(*a*) a simple, weak, aqueous solution of methylene blue; (*b*) 30 c.c. of a concentrated alcoholic solution of methylene blue, and 100 c.c. of solution of caustic potash (1 in 10,000); or (*c*) an aqueous, 2 per cent solution of methylene blue, mixed with equal parts of a 5 per cent solution of borax. To the dried and fixed blood on the slide a few drops of the staining fluid is added, allowed to remain for thirty seconds, when the stain is washed off with distilled water, and the specimen dried between layers of filter paper and held over the flame of a spirit lamp, and mounted in xylol balsam.

In specimens so prepared, the red blood corpuscles will be found unstained, while the parasites and the nuclei of the leucocytes are tinged blue.

The benign tertian parasite.—1. When the blood of a patient suffering from tertian fever, to whom quinine has not been administered, is examined some eight hours after the temperature attending a paroxysm of fever has fallen to the normal, the characteristic parasites may be seen within the red corpuscles. They occur as small, colourless bodies, changing, by amœba-like movements, to shapes resembling a disc, a star, a cross, or a ring. At first, pigment is not to be seen except occasionally, as a few irregularly distributed granules near the periphery of the parasites. 2. If a specimen of blood from the same patient is examined some eight hours later, it will be observed that the hyaline-looking bodies within the red corpuscles have increased in size, that the amœbic movements are more active, that the pigment has increased in quantity and activity, that the red corpuscle enveloping the parasite is paler in colour and has increased in bulk beyond its normal limits. 3. Were the blood of the same patient submitted to examination towards the end of the forty-eight hours' interval which characterises the disease, further important changes can be made out. The parasite has increased in bulk to such an extent that it is difficult to see the pale attenuated remnant of the distended red corpuscle. The pigment movement is arrested and its granules collect towards the centre of the organism in two or three clumps. The hyaline-looking surface of the parasite becomes more granular, and, commencing at the periphery and extending towards the centre, fine striations appear which finally cause a complete segmentation, dividing the parasite into twelve to thirty leaflets. This is no doubt a true segmentation, the whole process being connected with reproduction, and the resulting leaflets are the young spores. Finally, the red corpuscular tissue containing the parasite gives way and the spores and pigment escape into the liquor sanguinis. The free spores appear as hyaline protoplasmic spherules possessing a central refracting area. Although the process has not actually been observed, the free spores are believed in many instances to gain access to adjacent red corpuscles, where the phenomena of growth and sporulation are again proceeded with. Others of the parasites appear to increase in size, exhibit a dancing movement in their pigment, and after violent agitation throw out unpigmented flagella, which become detached and float away, losing themselves amongst the corpuscles.

When the blood of a person subject to malarial fever is examined, by one experienced in the microscopical phenomena of malaria, it is easy to state not only what type of fever prevails, but also to predict the hour at which the paroxysm may be expected. Segmentation occurs immediately before the paroxysm, and with the rupture of the containing red corpuscles, and the escape of the spores and pigment, it would seem

as though a toxic agent found its way into the blood, causing the signs and symptoms of an attack of ague or other form of fever.

When all the parasites in the blood mature at the end of forty-eight hours, tertian fever will result, but if a certain number mature twenty-four hours earlier than the remaining half, the fever will exhibit the quotidian type.

The benign quartan parasite.—When the blood of a patient suffering from the quartan type of malarial fever is examined within twelve hours after the subsidence of a paroxysm, a parasite will be found within the red corpuscles well-nigh indistinguishable from the pale amœbic body described as met with in the tertian type. When, however, the time for the recurrence of the paroxysm approaches, say sixty-two hours after the last attack, sufficiently marked differences are met with, which enable a conclusive diagnosis to be established by microscopical examination, whereby the quartan may be distinguished from all othe types.

The quartan, as compared with the tertian, parasite, (1) possesses a more definite outline; (2) the amœbic movements are slower; (3) the pigment is darker in colour and coarser; (4) segmentation begins some ten hours before the expected paroxysm, when some six to twelve leaflets (spores) only are formed. Subsequently the escaped spores behave, as regards occupation of other corpuscles and flagellation, as in the case of the tertian parasite.

When the quartan parasites, present in the blood, preserve the same stage of development, fever will recur every seventy-two hours. With quartan parasites exhibiting two cycles of maturation, paroxysms of fever will occur two days running, with a third day's freedom from pyrexia. This type is known as the "double quartan." When quartan parasites, presenting three groups of development, are met with, paroxysms of fever will recur daily—the "triple quartan."

Malignant or æstivo-autumnal parasites: the parasites of the irregular malarial fevers.—Three forms of parasite—(1) the pigmented quotidian; (2) the unpigmented quotidian; and (3) the malignant tertian—are associated with the so-called malignant types of fevers; and the crescent-shaped parasite, the "gamete"—sexual form—of the malignant tertian parasite. The differences between the benign and malignant parasites may be summed up as follows:—(1) The cycle of development of the parasites of the malignant type are not so clearly defined as is the case with the benign; it is believed to extend to twenty-four and forty-eight hours; (2) the malignant parasites do not mature in groups, but independently, as it were, some appearing in the early intra-corpuscular stage, whilst others are met in all stages up to complete maturation and sporulation in the same specimen; (3) the peripheral blood shows but little evidence of the presence of the segmenting parasites; they have to be searched for post-mortem in the deeper viscera, especially the

spleen and in the marrow of the bones; (4) in their earliest stages the benign and malignant parasites resemble one another closely, but later fairly well-marked features serve to differentiate them; in the malignant varieties the parasite is much smaller, rarely occupying more than one-third of the red corpuscle; the shape varies from a ring-like body with high refractive power and a central darker area to that of a hyaline mass endowed with active amœboid-like movements; these conditions may alternate once, twice, or thrice, the one shaped body changing to the other with alacrity; (5) the pigment is for the most part scanty; (6) the red corpuscle containing the parasite becomes crenate and wrinkled, and often assumes a dark green hue—the "brassy body" of some writers. Sporulation proceeds as in the benign forms, and the ultimate destination of the benign and malignant parasites seems analogous.

Crescent-shaped bodies.—In a case of remittent or continued malarial fever, which has lasted a week or more, the "crescent-shaped" body is to be met with, first in the blood of the organs, and later in smaller numbers in the peripheral blood. As the name implies, the parasite is crescent-shaped, and in the concavity of the arch stretching between the horns is to be seen the remains of the red corpuscular host, altered somewhat in shape and colour. The pigment may be either diffused through the mass of the parasite, or it may appear as rods collected into a central clump.

The significance of the "crescent" bodies is subject to several interpretations. Some have believed them to be a separate parasite, others that during the continuance of the fever a certain number of the recognised parasites, instead of sporulating, increase in size, acquire pigment, and destroy the red corpuscles they inhabit. They are now known to be the gametes of the malignant parasite. Manson's interpretation of the crescent bodies is, that, as they seem incapable of further development in the blood, and as they are passive agents so far as the appearance of fever is concerned, they are the means by which the "extra-corporeal" life of the parasite is maintained in media other than the human blood and body, and that their flagellation is a necessary part in the life-history of the parasite.

When crescent-bearing blood is exposed to the air for a few minutes, and examined microscopically, the crescent body, after some fifteen to thirty minutes, shows signs of activity. The pigment accumulates in the centre of the parasite, its granules dance about, and its whole body becomes agitated, until suddenly, from the circumference, flagella, two to five in number, shoot forth and lash about in restless activity. The flagella subsequently separate from the parasite, and move away amongst the corpuscles, leaving the parent body still and passive.

The part the mosquito plays as the "extra-corporeal" host of the plasmodium malariæ.—Several observers lay claim to the suggestion that the spread of malaria was in some way connected with mosquitoes.

Manson, however, was the first to put the theory on a scientific basis, and Major Ross in 1895 undertook the investigation of the subject practically. Manson was prompted in his contention by his investigations as regards the part the mosquito played in the life-history of the filariæ, and by his firm belief that the flagellation of the parasite after its removal from the body had a meaning and purpose. He believed that the mosquito, after extracting the blood of malarial persons, served as the host in which flagellation was carried on, and that this process was but one stage in the extra-corporeal life of the parasite. Ross, when he commenced his investigation, soon proved the truth of the initial stages by finding that in the mosquito's stomach 70 per cent of the crescent bodies developed flagella. For a time no further trace of the organism could, however, be found, until, after a long and patient search, the pigmented bodies characteristic of malarial infection were found in the walls of the mosquito's stomach. Not, however, in all mosquitoes, and it was only after lighting upon the "dappled-winged" and the "gray" mosquitoes that this phenomenon was discovered. Following the teaching and example of Professor M'Callum of the Johns Hopkin's University, U.S.A., Ross turned his attention to the parasites met with in the blood of certain birds. In the stomachs of birds ample proof was to hand of flagellation. The flagella were found to break away and impregnate, or at least occupy neighbouring cells, and produce melanin in quantity. The cells so impregnated Ross traced into the stomach walls of the mosquito, and observed that they protruded on the outer surface of the stomach towards the body cavity of the animal. Whilst this "coccidia"-like process was going forward, the protoplasm of the cells changed to rod-like bodies—sporozoids. In the body cavity Ross was able to find these dark rod-like bodies freed of their enclosing envelope, and scattered throughout the cavity and in the blood of the mosquito. Finally, they were found in what appeared to be the salivary or poison glands of the mosquito, and even in the ducts of these glands leading to the proboscis.

Inferring that these rods might be the infective medium, Ross next subjected healthy birds to mosquito bites, and had the satisfaction of finding the developed parasite in the blood of these birds after an incubation period of from five to nine days. So far as bird and mosquito relations go, the cycle of their parasites has been proved, and the facts accumulated around the human malarial parasite seem to indicate an analogous, if not an identical process. In fact Grassi, Bastianelli, and Bignami, have lately proved by direct experiment this phenomenon also in man.

The parasite.—The anatomy of the parasite is most readily studied when subjected to staining by the boro-methylene method. It is then seen to possess a deeply-stained nucleolus, a clear, unstained, vesicular nucleus, and a lightly-stained protoplasmic surrounding.

The melanin.—The pigment met with in malaria is derived from the disintegrated hæmoglobin. It resists the action of strong mineral acids; it is decolorised by ammonium sulphide in solution, and also by free alkalies. Although derived from so richly hæmatinic a substance as hæmoglobin, no iron is found in its composition.

Phagocytosis.—Many leucocytes in the blood of persons suffering from any form of malarial fever are seen to contain either one or more of the parasites, or the leucocyte may engulf the parasite and the red corpuscle containing it. The power of the phagocytes to attack foreign elements in the blood extends also to the flagellæ and flagellate bodies, and in many the melanin granules are all that is to be seen to represent what once was a living parasite. The phagocytes have no doubt a salutary influence, and were they in sufficient numbers to cope with the influx of parasites, they would annul their baneful effects entirely. It can easily be believed that the blood of all persons living in a paludal area is infected to some extent by the prevailing parasite, and it is in the power of the phagocytes, by their scavenging properties, to afford protection or so-called immunity. The writer has found phagocytes in numbers in the blood of healthy persons dwelling in malarial districts, but when fever seized them the phagocytes almost entirely disappeared, to re-appear once more as the paroxysm subsided.

Clinical features of malarial infection.—I. INTERMITTENT FEVERS.—Quotidian, tertian, and quartan fevers exhibit the three stages characteristic of ague.

(1) *The cold stage* is ushered in by a feeling of lassitude, frontal headache, yawning and stretching, or a feeling of nausea. Soon the patient looks cold and feels cold, and a violent rigor supervenes. The skin is cold to the touch, but the temperature of the mouth, or more marked still that of the rectum, is raised from the first, and speedily rises, even during the rigor, to the maximum 105° or 106°. The cold stage may last from a few minutes to an hour or more.

(2) *The hot stage.*—The skin during the hot stage is dry and burning to the touch, the face flushes and the pulse strikes full and strong. The patient desires to be rid of warm covering, and complains of intense thirst, a throbbing headache and pains in the limbs. Delirium, characterised usually by a rambling talk in adults, and not unfrequently accompanied by convulsions in children, is not uncommon. The hot stage continues for an hour or two and bears an inverse ratio to the cold stage; the shorter the cold stage the longer the hot and *vice versâ*.

(3) *The sweating stage.*—With the appearance of profuse perspiration the restlessness and pains subside, and after free perspiration for two or three hours the paroxysm is over.

Strictly speaking there is no such disease as a quotidian ague; as already explained, the daily recurrence of fever is either a double tertian or a triple quartan. The typical intervals of the regular intermittent are twenty-four, forty-eight, and seventy-two hours; when succeeding attacks appear earlier than the typical times the fever is said to "anticipate"; when, on the other hand, the period is delayed the fever is said to be "postponed." The latter type is regarded as evidence of abatement in severity. After a paroxysm of fever is over the temperature falls considerably below the normal, and according to the excess of the high temperature so is the fall proportionate. The writer estimated, from a careful study of many temperature charts, that for every degree of rise above the normal there was a corresponding fall of one-eighth of a degree below the normal, after allowing for the diurnal rise and fall of health.

II. Remittent fever. — At the onset remittent fever is attended by a feeling of dullness which may extend over several days, or it may be ushered in by a sharp rigor. The usual initial signs and symptoms of "feverishness" are present, and these are followed by a heightened temperature, which continues with but slight abatements or remissions. Abortive attempts at sweating may occur, accompanied by a corresponding decline of the body heat, but the temperature does not fall to the normal. So persistently is the fever maintained in some cases that the fever is named "continuous" or "continued" fever. When vomiting is severe the name "bilious remittent" is employed to designate the type. Other names, such as "gastric and typhoid remittent and typho-malarial fever," indicate the resemblance of the remittent type of malarial fever to typhoid. So pronounced is this at times that it is only by examination of the blood and the evidence of a carefully kept temperature chart that the diagnosis can be established. Many, if not most of the so-called aborted typhoids may be real remittents. There is no doubt we have in the tropics a fever which is wont to follow a weekly cycle. Should quinine prove of uncertain benefit after a two or three days' trial, and the fever, if malarial, be left to run its course, it will end on either the seventh or the fourteenth day. So persistently did these dates of subsidence occur in the practice of the writer, that he termed them a one week, a two week, and even a three week fever, and by observing the behaviour of the temperature during the first two or three days of the illness, it was possible to predict the day of its prospective fall.

In the blood of persons suffering from remittent fever the malignant or æstivo-autumnal parasite is found; and after the

fever has lasted one week the crescent-shaped bodies are to be seen.

III. Irregular forms of fever are also associated with the presence of the malignant parasite in the blood. When intermissions are short and the paroxysms long, extending even to twenty hours or more, these fevers form a connecting link between true intermittents and the remittent group.

IV. Pernicious malarial fever.—When any one organ, or group of organs, is singled out to bear, as it were, the intensity of the attack of fever, and the organ is seriously affected, the name "pernicious" is applied to the condition. (*a*) In the cerebral, comatose, or apoplectic type the nervous system is so severely implicated that unconsciousness supervenes and the patient may die in coma; (*b*) algide malaria attacks the gastro-intestinal tract so violently that the symptoms resemble those of cholera; (*c*) should the kidneys have to bear the brunt of the paroxysm, hæmaturia may be present.

V. Long interval fevers.—It is not uncommon to meet with patients who get attacks of fever at intervals of months or years, or who have recurrences of fever long after they have settled in a non-malarial country. In fact, many tropical residents never get an attack of fever until they take up their abode in a temperate or cold climate. In such cases the parasite attains a "latent phase" and develops into activity only after its human host has been exposed to some severe mental or bodily strain.

The effect of malarial infection. — Anæmia and enlarged spleen are the two prominent conditions set up by long-continued exposure to paludal infection. Anæmia is regarded as a constant result of residence of Europeans in tropical countries; and in all probability this is to be ascribed, in the majority of instances, even in persons who have never had ague or remittent fever, to the direct action of the malarial parasites on the blood corpuscles, rather than to the effect of mere "climate."

With each paroxysm of fever the red corpuscles decrease in number. Instead of the normally estimated 5,000,000 red corpuscles in 1 cubic mm. of the blood, oligocythæmia may proceed to such an extent that their number may be reduced to one-fifth or even one-tenth of the normal quantity. It is estimated that in each cubic mm. of blood 1,000,000 red corpuscles may disappear in a single paroxysm.

Poikilocytosis, more especially in fevers of the malignant types, is to be observed, the red corpuscles showing numerous differences in

shape. Not only is the actual quantity of *hæmoglobin* diminished, but after continued recurrences the remaining hæmoglobin is lessened in physiological value.

Malarial anæmia is characterised by the usual pallor of the skin and mucous membranes, and the attendant circulatory, digestive, and renal troubles. Vitality is markedly lowered and the spirits subject to fits of serious depression.

The *liver* is to be found enlarged and somewhat tender, and the *spleen* in all chronic malarial affections increased in bulk, it may be to an enormous extent.

Post-mortem appearances. — In addition to evidence of anæmia, parasitic infection of the red corpuscles and widely spread pigmentation, the following conditions are met with.

The *spleen* is enlarged at times so that it weighs several pounds, and the splenic tissue, when death has resulted after long-standing illness, is dark-gray in colour, and firm in consistence. Microscopically examined the melanin will be seen to occupy the trabeculæ and blood-vessel walls, and the macrophages are deeply pigmented. The *liver* is usually somewhat enlarged, the tissue is of a dark gray colour, and microscopically the capillary walls and the phagocytes are found to be loaded with parasites. Cirrhosis is sometimes met with, or again small necrotic areas are seen scattered through the liver substance.

The *kidneys*, in addition to their darkened colour, are somewhat enlarged, and in the glomeruli pigment is readily detected.

The *peritoneum* and the mucous membrane of the *alimentary canal* from the stomach to the rectum is stained a slate-gray colour.

The *brain* appears darkened in colour, and in the red corpuscles in the capillaries are seen parasites in large numbers. Even the endothelial lining of the capillaries is found swollen and pigmented. The *marrow of the long bones* becomes almost black, as the result of prolonged malarial infection. Macrophages similar to those met with in the spleen are found loaded with pigment, and in the marrow itself pigmentary masses are not uncommon.

Prognosis. — The prognosis in the case of benign forms of fever, so far as the life of the patient is concerned, is good, but repeated attacks may so enfeeble a patient the subject of malaria that a chronic cachexia of very grave import may supervene.

The malignant malarial fevers are attended by considerable direct danger to life, and paroxysm may succeed paroxysm, leading to fatal results. When pneumonia, dysentery, or nephritis complicate malarial infection, the prognosis is grave indeed. Malarial

cachexia tends to disappear after the patient has spent a couple of years in a healthy non-malarial locality; but any subsequent illness is liable to assume features of a malarial type. Several forms of neuritis and paralysis are ascribed to malaria; these also tend to disappear when the malarial district is left behind.

Prophylactic measures.—I. *Personal prophylaxis* consists of—avoiding chills, changing damp clothing at once, sleeping under mosquito netting and not on the ground level, moderation in eating, drinking, and smoking, wearing flannel next the skin, and protecting the head by a sun hat. Loss of sleep, fatigue and mental anxiety conduce to pave the way for incursion of fever.

II. *Medicinal prophylactic measures* resolve themselves into the taking of quinine. Quinine should be taken before going out of doors when the place of temporary residence is known to be highly malarial, or when the season of the year predisposes to attack. Five grains is the usual dose, but if the drug has to be continued for several weeks three grains will be sufficient. Plehn holds that five grains every fifth day is ample protection. When a person living in a malarial district is over-fatigued, catches cold, or is run down from any cause, a five-grain dose of quinine taken immediately may prevent evil consequences resulting.

III. *General prophylaxis.*—Subsoil drainage is the only known expedient of public sanitation which can be said to directly and primarily affect the prevalence of malarial fever. Cultivation of the soil, planting trees, especially, it is averred, the eucalyptus tree, the supply of good water, and the improvement of house and town drainage are important adjuncts. From what we know of the mosquito, its habits and its proved connection with the life of the malarial parasite, boiling the water used for drinking, cooking, and even for bathing purposes is a safe precaution. The anopheles species of mosquito is the insect which has so far been accredited as the intermediary host of the malarial parasite. The ova of the insect are deposited in shallow, stagnant pools, and there the mature insect is developed. Local prophylaxis consists in sweeping out these pools or in covering the water by kerosine, turpentine, or other oily substances.

Treatment.—During the paroxysm of malarial fever the patient should, whenever possible, get into bed. Flannel should be worn and the linen sheets dispensed with. During the cold stage hot-water bottles and extra blankets are necessary, and warm drinks of weak tea, hot water and freshly-made lemonade are comforting. During the hot stage the patient must be prevented throwing off the

extra clothing to too great an extent, and warm drinks are to be freely supplied unless vomiting supervenes, when ice may be given to suck. When the sweating stage arrives the hot bottles must be removed from the bed, the excess of covering reduced, and if the pulse is weak a stimulant may be given with the warm drinks. After the temperature has fallen to the normal the surface of the body should be wiped dry, and fresh flannels and blankets supplied.

Antipyretic remedies of the nature of antifebrine, antipyrin, and phenacetin are largely used in the treatment of malarial fevers. Unless, however, the temperature during the hot stage becomes excessive there is no justification for their use. They no doubt procure a freer perspiration, but it is improbable that they curtail the period of the paroxysm. When, however, the temperature, in adults more especially, rises above 105°, phenacetin is perhaps the safest of the specially antiphlogistic remedies, and it may be given in ten-grain doses every twenty minutes until thirty grains are given. The same rule may be followed with antipyrin, and it is wise with each dose to give a drachm or two of brandy. The writer has had excellent results with the hypodermic injection of antipyrin, on one occasion reducing a temperature of 107.6° in twenty minutes to 103°, and in twenty minutes more to 100° by a hypodermic of five grains of the drug. Should other means fail, resort may be had to the wet pack, or to baths in which the temperature is gradually reduced from that of the body warmth to extreme coolness by the addition of ice to the water.

Medicines.—The medicinal treatment of malarial diseases, be the variety what it may, is quinine; whether as the sulphate, the bisulphate, or the hydrochlorate is, for the most part, a question of choice. It may be administered in solution with a few drops of mineral acid, in tabloids, in powders, or hypodermically; quinine in the form of pills, more especially when coated, is to be avoided. The amount of quinine to be exhibited need not be excessive; a fifteen-grain dose to start with, followed by five grains every four hours, is sufficient, the interval and amount of the dose increasing and decreasing respectively as the symptoms and paroxysm abate. The time of administration is of some consequence; in intermittent fevers the period of apyrexia is selected and the drug continued up to the onset of the paroxysm. In remittent fevers and in those of the more continuous type quinine must be given at regular intervals without regard to decline in temperature. It is possible that antiphlogistic medicines—antipyrin or phenacetin causing a lowering of the temperature and sweating—may be employed with some

advantage, the quinine being given during the temporary abatements. It may be taken as an axiom that, if quinine in five-grain doses has been administered every four hours for three days without decided effect, the case is most certainly not one of malaria. When vomiting annuls the giving of quinine by the mouth it may be injected hypodermically. The soluble hydrobromate or lactate of quinine, or the bisulphate, may be used dissolved in tartaric acid (five grains of tartaric acid dissolving thirty grains of the sulphate). A fifteen, twenty, or even thirty-grain dose of either of these drugs may be injected into the subcutaneous tissues or into the substance of the muscles. Quinine is accused of possessing several disadvantages; headache, delirium, deafness, hæmaturia, hæmoglobinuria, gastro-intestinal derangements, etc., are laid to its charge, for the most part, if not wholly unjustifiably. The most untoward objection is the tendency to a deep-seated abscess and wide destruction of the skin after hypodermic injection. Opium is a favourite drug in many countries, and hypodermic injections of morphia, by allaying feelings of malaise and nausea, have many advocates as accessories to quinine. When pernicious fever assumes the comatose, algide, or cerebral types, suitable remedies must be promptly adopted. Food must be administered by the rectum if necessary; heart failure must be combated by stimulants and hypodermics of either atropin or strychnine. Of prepared remedies Warburg's tincture is by far the most reliable and beneficial; methylene blue, arsenic, eucalyptus, ergot, etc., etc., are used by but few practitioners. Euchinin, the ethyl carbonate of quinine, also finds some supporters.

Malarial cachexia is best treated by removal of the patient to a non-malarial district. A temperate or even cold climate is most advantageous for invalids suffering from chronic tropical malaria. Towns and the sea-side are to be avoided, and prolonged residence on high ground is imperative if speedy and thorough recovery is desired. Drugs, when cachexia is marked, are of little avail. Arsenic and iron serve as adjuvants at times, and at times iron does harm. Enlargements of the spleen, if recent, disappear, but a chronically enlarged spleen may defy both internal and external remedies to reduce its size.

James Cantlie.

HÆMOGLOBINURIC FEVER

Syn. Blackwater Fever, West African Fever

A specific fever restricted in its geographical distribution and characterised by the presence of hæmoglobin and its derivatives in the urine.

Geographical distribution.—The disease is especially prevalent in the river basins of Equatorial Africa, but is also well known in the Western Hemisphere, in Cuba, Venezuela, and the Southern States of North America. It has been met with in a more sporadic form in East Africa, especially in the Zambesi basin; in Europe it has been seen in Italy and in Greece. Cases have been reported from India, Java, New Guinea, and the writer met with a well-marked case in Hong-Kong occurring in a medical man recently arrived from the gold-fields of Siam. Blackwater fever may occur after the patient has left the countries in which it is endemic.

Etiology.—Three beliefs obtain at the present day as to the cause of blackwater fever.

(1) That it is of malarial origin. In favour of this contention it is argued that the disease occurs only in those who have suffered from and are broken down by malaria. The parasites of malaria are usually met with in the blood, and all the features of a malarial paroxysm accompany blackwater fever.

Against this view, it must be stated that Laveran's parasite is not invariably found in the blood of persons suffering from hæmoglobinuric fever; that in some rare cases the disease may occur within four or five weeks after landing on the West Coast of Africa, and before malaria has had time to cause either anæmia or cachexia; that the very limited geographical distribution of the disease betokens either a special form of the malarial infection, or a toxic agent independent of the malarial parasite.

(2) Quinine is adduced as a causative agent. The chief reason for this belief no doubt lies in the statement that the administration of quinine, in large doses, seems to cause a recurrence of hæmoglobinuria in those who have become the subject of the disease. This may be a clinical phenomenon, but it is hardly worthy of being accepted as a pathological axiom. Malaria is so general and the administration of quinine in large doses so universal in

warm climates, that, were quinine in any way a determining cause of the disease, the geographical distribution of hæmoglobinuria would not be confined to a few definite and restricted regions. That quinine may do harm during a paroxysm, or may induce a relapse, is beside the question of the etiology of the disease.

(3) A specific agent is claimed by many observers as the cause of blackwater fever. For this belief there is much to be said; every scientific inference points in this direction. Laveran's parasite may be, and no doubt is associated with the disease, but the association may be, and probably is, nothing more than a means whereby the patient's strength is reduced and he becomes thereby liable to infection by the specific agent of hæmoglobinuria.

Dr. Sambon holds the opinion that the hæmoglobinuric fever in man is caused by a parasite similar to that which causes the hæmoglobinuric fever of cattle; in other words, its specific agent belongs to that group of hæmosporids which multiply by simple binary division. He further believes that paroxysmal hæmoglobinuria stands to blackwater fever in the same relation as enterocolitis (the dysentery of northern latitudes) to tropical dysentery, the difference in mortality arising from the fact of blackwater fever usually supervening on persons already weakened by tropical malaria.

Symptoms. — Hæmoglobinuric fever is often preceded or accompanied by symptoms of malarial infection.

It is seldom until after the first year of residence in a blackwater fever country that the disease develops, and the third year is considered to be the most likely period of its appearance. At any time during the second and third years of residence, during what seems to be a relapse of an irregular attack of fever, the patient is seized with marked rigors, accompanied by headache, pain in the loins, numbness in the extremities, pain in the epigastrium, and distressing vomiting of bile-stained fluid. The temperature suddenly rises to 103° or 104° F., the pulse becomes quick and small, the breathing increases in frequency, and the patient is restless, anxious, and apprehensive. The urine has at first merely a red hue, but speedily acquires a dark-brown colour and a thickened consistency; calls to micturate are frequent, often attended with pain, and more especially if the urine is scanty. When the fever has lasted some hours the conjunctivæ and the skin generally assume a yellow tint, caused in all probability by the acute hæmolysis which is taking place. After eight to twelve hours in favourable cases the temperature falls rapidly, with profuse and exhausting perspiration,

to below the normal, the urine soon clears, and all the aches and pains disappear. A trace of albumen may remain in the urine for some days and the patient continues in a weak state for a considerable time.

It may happen that no subsequent recurrence takes place, but more often on the following day all the signs and symptoms are repeated, or, on the other hand, the feverish attacks resembling malarial paroxysms may occur without the accompanying alterations in the urine.

Pathology.—The blood in blackwater fever usually indicates a pronounced anæmia. The red corpuscles show advanced poikilocytosis, their shapes being multiform. All the red corpuscles appear blanched as if deprived of their hæmoglobin. Leucocytosis is also a feature of the blood of blackwater fever, the polynuclear cells being especially increased in numbers. The whole of the hæmoglobin-producing powers of the blood appear to be concerned in the process, and it would seem, as suggested by Manson, that some toxic solvent agent is at work, whereby not only the disintegrated corpuscles, but also the uninfected red corpuscles, by being despoiled of their hæmoglobin, contribute to the urinary feature. When the urine passed during a paroxysm of blackwater fever is allowed to stand a sediment results, which, when examined, shows granular and pigmentary amorphous matter, large granular casts of hæmoglobin, some hyaline casts, a few red blood corpuscles and epithelial scales.

The viscera are not characteristically affected. Black pigmentary deposits are seen in the situations characteristic of malarial infection; the kidneys show cloudy swelling of the cells lining the tubules, the tubes are blocked, and yellow and black pigments are met with everywhere, except in the Malpighian corpuscles. The spleen and liver cells are similarly affected as regards pigmentary deposits, both black and yellow.

Staff Surgeon-Major Stendel of the German Army made an examination of the blood by means of Fleischl's hæmometer, and found that the amount of hæmoglobin present oscillated between 50 and 21 per cent of the normal standard. In two other cases the quantity was too small to be determined (*Lancet*, July 27, 1895, p. 225) by the instrument, but it was estimated by the observer at not more than 5 and 8 per cent respectively. He lays stress upon the prognostic value of hæmatological examinations.

Diagnosis.—Yellow fever is the disease with which blackwater fever is most apt to be confounded. In yellow fever the urine

contains albumen at an early stage and without hæmoglobin; in blackwater fever it contains cell-globulin, not albumen, and only when dark in colour from hæmoglobin. Dark urine is an early feature in blackwater fever. The vomited matters are not merely the bile-stained fluid met with in hæmoglobinuria, but consist of the disintegrated red corpuscles and coagulated blood. Neither the spleen nor liver are enlarged in yellow fever, and post-mortem evidence of pigmentation is wanting.

But hæmoglobinuria may be caused by organic or inorganic toxins, such as potassium chlorate, arseniuretted hydrogen, sulphuric acid, hydrochloric acid, phenol, naphthol, aniline, chrysarobin, pyrogallic acid, etc., and by the influence of cold or arduous muscular exertions. The diagnosis between hæmoglobinuria arising from such causes and blackwater fever is made, however, without difficulty. The paroxysmal hæmoglobinuria of temperate climates in many respects resembles blackwater fever, but it is rarely a fatal disease. Moreover, it is a disease but occasionally met with over widely diffused areas. The blackwater fever of West Africa (and elsewhere) is, however, a frequent ailment in these regions, and may be attended by a mortality as high as 60 per cent of those attacked.

Prognosis.—A single attack of blackwater fever may be followed by complete recovery. Repeated attacks may in like manner result in disappearance of the malady. When, however, the disease persists, when remission and not intermission of symptoms prevail, when the urine becomes scanty or is suppressed, a grave prognosis is called for. Recovery, however, takes place from what seems well-nigh hopeless conditions.

Unfavourable symptoms are a continuance of high fever, persistent vomiting, purging of marked severity, suppression of urine, mental depression, restlessness and delirium, deepening of the jaundiced hue, a dry tongue, and a feeble pulse. Symptoms of uræmia usually precede a fatal termination.

Treatment.— During the paroxysm of blackwater fever quinine should be withheld. Attempts must be made to allay excessive retching by giving ice to suck, and by mustard plasters over the epigastrium. Strength must be maintained by rest in bed, by giving sips of brandy and water or champagne, by ether hypodermically, by rectal nutritive enemata, etc.

Perspiration should be encouraged by any of the usual methods. The writer has found good results from the administration during the attack of ten drops of oil of turpentine every two or three hours.

When blood examinations show the presence of the malarial parasite, quinine must be resorted to when once the paroxysm of blackwater fever has abated. Should repeated attacks of hæmoglobinuria recur coincidently with the administration of quinine, the drug must be withheld, and the patient removed, if possible, from the district where the disease is endemic to a temperate climate.

The nephritis which sometimes accompanies an attack of blackwater fever must be treated on general principles.

JAMES CANTLIE.

KALA-AZAR

An epidemic communicable disease, probably malarial in nature, characterised by an acute onset and recurrent accessions of fever, by enlargement of spleen and liver, by anæmia and cachexia, and by a high death-rate. The disease has been accurately observed in Eastern Bengal and Assam only.

Kala-dukh and kala-jwar, met with in the Purnea (Bengal) and Darjeeling districts respectively, are, in all probability, kala-azar under different names.

Etiology.—Considerable divergence of opinion concerning the cause of kala-azar has up to the present obtained, nor can it be considered that the question is yet settled. The first systematic inquiry into the etiology of the disease was made by Major Giles, I.M.S., who believes kala-azar to be "a mixed anæmia brought about by ankylostomiasis acting on a population worn down by chronic malarial poisoning." Captain Rogers, I.M.S., as the result of his investigations made subsequently to Major Giles's report, came to the conclusion that kala-azar is malarial in origin. Against the theory of the disease being ankylostomiasis it may be urged that ankylostomiasis is so widespread, not only in Assam, but also throughout India, the Malay Peninsula, and the Archipelago that it is improbable so definite a set of symptoms as are described under the kala-azar of Assam could be set up in one district only, and, as far as we know, be unobserved in the others.

We are indebted to Major Ronald Ross, I.M.S., for extending and systematising our knowledge of the disease. In his masterly report upon "The Nature of Kala-azar" to the Government of

India, published in 1899, occurs the following statement: "That Kala-azar is malarial fever in which the original invasion gradually dies out during the first stage of the disease, leaving, in the second stage, an acute tumour of the spleen and liver accompanied by a constant secondary or symptomatic fever, and finally resulting in a cachexia in the third stage."

Although the initial symptoms of kala-azar, which prevail in malarial districts, are almost, if not quite, identical with those of malarial fever, yet against the malarial theory of the nature of the malady the following points have to be considered:—the existence of a low constant fever not amenable to quinine, and totally unlike malarial fever in the second stage of the disease: the apparent absence of the parasites and melanin of paludism, both during life and after death, from many established cases of the disease; the communicability of kala-azar from the sick to the healthy; its epidemicity and its high death-rate.

The evidence derived from post-mortem examinations points to death by typical paludism, as far as the liver, spleen, and kidneys are concerned. The structure of these organs is practically unaltered, there being no neoplasms or necrotic areas. Melanin, however, is absent or in minute quantity. Yellow pigment prevails, but that is frequently due to a variety of agencies.

Symptoms. *First stage.*—Kala-azar is ushered in by a marked rigor and fever of a severe nature. The fever at first is remittent in nature, but soon becomes intermittent; and, in the majority of cases, rigors usher in the recurrent accessions. After the initial fever, which lasts from ten days to twenty-one days, a period of apyrexia usually supervenes, which may continue for weeks or months, when a succession of relapses may occur, the fever in each case resembling the initial, except that there may be no rigors. On the other hand, a continued low fever is established in many cases soon after the primary attack, and continues throughout the period of infection.

Enlargement of the spleen and liver are met with from almost the first onset of the fever. The spleen is tender to palpation, and quickly increases in size. Anæmia and even emaciation may appear during the first stage so rapid is the blood change, and it is this quickly supervening anæmia which gives rise to the dark leaden appearance of the features and skin, which serves to give the name to the disease—"kala" signifying black or deadly.

The second stage.—When the fever assumes a constant low type and the spleen enlargement is established, the second stage of

the disease is said to commence. In regard to the temperature the diurnal curve remains the same day after day for weeks or even months. If between 96° and 99° one day, the temperature chart on succeeding days, for weeks or months, will show the same; or should the range be between 98° and 102°, the same obtains, showing but a small range of variation. The splenic dulness may occupy most of the left half of the abdomen, and the liver exceeds its normal limit downwards by from 2 to 3 inches. On percussion both organs exhibit signs of tenderness. Anæmia is pronounced, but not excessive, during the second stage of the fever. Emaciation is usual; and epistaxis, ascites, œdema of the feet, and sometimes of the face, are commonly met with, and a slight degree of icterus is frequently noted.

Third stage.—When the abdominal organs lose their tenderness, when their enlargement ceases and fever declines, the third stage is said to commence. Cachexia is the marked symptom of this period. Ascites and occasionally œdema of the feet continue, and diarrhœa, dysentery, and pneumonia are wont to supervene. The patient may succumb to asthenia, or he might recover; but when cachexia is once firmly established recovery would seem to be impossible.

The duration of the first stage is usually from one to two months, and the beginning of the third stage occurs nine months or more after the commencement of the illness.

Diagnosis.—Kala-azar can only be diagnosed when it has reached the second stage of its course. Before this period is reached ordinary paludism, beri-beri, and the anæmic state resulting from ankylostomiasis, have all been mistaken for it.

Prognosis.—"The death-rate is high, but recovery often occurs" (Ross). Death takes place occasionally during the second stage of the disease, but it is the third stage during which marked fatality occurs.

Treatment.—Most observers maintain that quinine is not only useless, but even harmful in kala-azar. The first duty of the practitioner is to examine the stools for the ova of the ankylostoma and, if present, administer the appropriate remedies for their expulsion. This step is taken not in the belief that the ankylostoma are the cause of the disease, but in order to remove the lowering tendency a number of intestinal parasites have on the general health. Further treatment consists in maintaining the patient's strength, counteracting the anæmia, relieving the ascites, and obtaining, if possible, a change of air.

JAMES CANTLIE.

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